



What drives patients with sleep, anxiety or depressive disorders to seek care from general practitioners with preference for homeopathy and other complementary medicines? Results from the EPI3 population survey." A cross sectional study".

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STROBE Statement—Checklist (cross-sectional studies): ‘What drives patients with sleep, anxiety or depressive disorders to seek care from general practitioners with preference for homeopathy and other complementary medicines? Results from the EPI3 population survey’ by Lamiae Grimaldi-Bensouda et al.

	Item No	Recommendation	
Title and abstract	1	(a) Indicate the study’s design with a commonly used term in the title or the abstract	✓
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	✓
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	✓
Objectives	3	State specific objectives, including any prespecified hypotheses	✓
Methods			
Study design	4	Present key elements of study design early in the paper	✓
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	✓
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants	✓
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	✓
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	✓
Bias	9	Describe any efforts to address potential sources of bias	✓
Study size	10	Explain how the study size was arrived at	✓
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	✓
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	✓
		(b) Describe any methods used to examine subgroups and interactions	✓
		(c) Explain how missing data were addressed	N/A
		(d) If applicable, describe analytical methods taking account of sampling strategy	N/A
		(e) Describe any sensitivity analyses	N/A
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	✓
		(b) Give reasons for non-participation at each stage	✓
		(c) Consider use of a flow diagram	N/A
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	✓
		(b) Indicate number of participants with missing data for each variable of interest	N/A
Outcome data	15*	Report numbers of outcome events or summary measures	✓
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted	N/A

		estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	
		(b) Report category boundaries when continuous variables were categorized	N/A
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	N/A
Discussion			
Key results	18	Summarise key results with reference to study objectives	✓
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	✓
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	✓
Generalisability	21	Discuss the generalisability (external validity) of the study results	✓
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	✓

Symbols: ✓, checked; N/A, not applicable.

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

What drives patients with sleep, anxiety or depressive disorders to seek care from general practitioners with preference for homeopathy and other complementary medicines? Results from the EPI3 population survey. “A cross sectional study”.

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Keywords: anxiety disorders; affective disorders, unipolar depression; sleep disorders; epidemiology; quality of life.

Word count: 3559

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3 **Abstract**
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7 **Objectives:** To assess the determinants in patients with sleep, anxiety or depressive disorders (SADD)
8 seeking care from general practitioners (GPs) with different practice preference towards
9 conventional medicine (GP-CM), mixed complementary and conventional medicine (GP-mixed), or
10 strictly homeopathy (GP-Homeo).
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15 **Design and setting:** The EPI3 survey was a nationwide, observational study of a representative
16 sample of general practitioners and their patients, conducted in France between March 2007 and
17 July 2008.
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21 **Participants:** 1572 patients diagnosed with SADD.
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24 **Results:** Patients attending GP-CM and GP-Mixed showed similar profiles whereas GP-Homeo
25 patients had healthier lifestyles. Psychotropic drugs were more likely to be prescribed by GP-CM
26 (64%) than GP-Mixed (55.4%) and GP-Homeo (31.2%). The three groups of patients shared similar
27 SADD severity.
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32 **Conclusion:** Despite their different characteristics, belief in CAM and lower psychotropic drugs
33 prescription, patients with SADD who consulted a GP-Homeo had similar quality of life to those
34 attending a GP-CM. Knowledge of these patterns may help to better plan resource allocation and
35 management of these diseases in primary care.
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43 **Article summary**
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50 **Article focus**
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- 52 • Up to 20% of patients attending primary healthcare in developed countries suffer from the
53 often linked anxiety and depression disorders.
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- Conventional treatments, particularly antidepressants and anxiolytics, are widely prescribed; often associated with adverse side effects, conventional treatments are a likely cause for an increasing number of patients to choose homeopathy and other complementary therapies.
- Understanding the characteristics of physicians and patients, from prescribing or using homeopathy, respectively, in conjunction with or instead of psychotropic drugs is undoubtedly of clinical and public health relevance.

Key messages

- Our results suggest that patients experiencing SADD who chose a GP with a clear orientation towards homeopathy, differed in their socio-demographic profile but not in the severity of their mental illness from those attending regular GPs with prescribing preferences towards conventional psychotropic drugs.
- Our survey is one the few studies highlighting that sleep, anxiety and depressive disorders show similar burdens in terms of severity and impact on mental impairment regardless of GPs' prescribing preferences.
- Our results showed that patients with SADD, whilst differing principally in their socio-demographic profiles and conventional psychotropic prescriptions, were actually rather similar regarding the severity of SADD in terms of comorbidities and quality of life.

Strengths and limitations

- Strengths of the EPI-3 study include high representativeness of the patients involved and comparability against other nationwide studies.
- The main limitation of our study relates to the classification of GPs, which relied on self-reporting of CAM prescriptions; generalisations from the results must be therefore made cautiously since our findings relate to general practice in France.

INTRODUCTION

Mental health problems such as sleep, anxiety or depressive disorders (SADD) are responsible for considerable disability worldwide[1] resulting in serious quality of life impairment[2] and are often associated with high use of medical services. It is estimated that up to 20 percent of patients attending primary healthcare in developed countries suffer from the often linked disorders of anxiety and depression. A high prescription rate of conventional therapies, particularly antidepressants,[3,4] which are often associated with adverse side effects, are a likely cause for an increasing number of patients to choose homeopathy and other complementary therapies.[5]

Evidence of effectiveness of these therapies compared to conventional psychotropic drugs is still limited.[6-8] Nonetheless, their perceived safety may be an important factor motivating patients with SADD disorders to seek care from GPs preferring homeopathy and other complementary medicines. Among complementary alternative medicine (CAM) modalities of practice, homeopathy is widely used in countries with large access to CM and represents a particularly good marker for CAM practice in France, where homeopathic drugs are partly reimbursed by national health insurance and prescribed only by a medical practitioner, if not purchased as over-the-counter drugs.[9,10] In a previous study,[11] homeopathic practitioners (including non-medical healthcare professionals) indicated that their patients used homeopathy mainly in association with conventional psychotropic treatments, psychotherapy and counselling in a mixed practice.

Understanding characteristics of physicians and patients, prescribing or using homeopathy, respectively, in conjunction with or instead of psychotropic drugs is undoubtedly of clinical and public health relevance. The objective of this study was to assess the motivations driving patients with SADD to seek care from general practitioner (GP) with different prescribing preferences in primary care, such as strictly conventional medicine (GP-CM), mixed complementary and conventional medicine (GP-mixed), or strictly homeopathy (GP-homeo).

METHODS

Study design, settings and participants

The EPI3 survey was a nationwide, observational study of a representative sample of general practitioners and their patients, conducted in France between March 2007 and July 2008. The methodology of the study has been described elsewhere.[2]

Participants (GPs and their patients) were drawn by applying a two-stage sampling process. The GPs were first randomly selected from the French national directory of physicians and invited to participate, which meant allowing a research assistant to conduct a one-day survey in the waiting room at the doctor's practice. Blind to the study focus on conventional and complementary alternative medicines (CAM) practice, consenting GPs were next contacted by telephone to enquire how frequently they prescribed CAM (homeopathy, mesotherapy, acupuncture, phytotherapy, etc.). Depending on their prescribing preferences towards homeopathic medicines, they were classified as: strictly conventional GPs (GP-CM), who declared themselves never or rarely using CAM or homeopathic medicines; mixed practice (GP-Mixed), who were GPs declaring using CAM regularly; and registered family homeopaths (GP-Homeo), who prescribed mainly homeopathic treatments. In France, homeopathy can only be prescribed by physicians, mostly GPs qualified as homeopaths by the French National Council of Physicians (CNOM) upon completion of specific training (3.3% of all French GPs in 2008).[12]

The second stage of selection consisted of random one-day sampling of consultations per participating physician, in order to survey all patients attending the practice on that very day. All adults (over 18 years old) and accompanied minor patients were eligible for inclusion in the EPI3 survey, except those whose health status or literacy level did not allow responding to a self-administered questionnaire.

During the consultation, GPs asked all adult patients diagnosed or suspected of suffering SADD whether they would volunteer for a more in-depth study of their disease. Consenting patients were contacted again within 72 hours for a telephone interview conducted by trained interviewers.

Data collection

Collection of data from patients included: age, gender, nationality, educational attainment, type of health insurance, additional private insurance, smoking habit, alcohol intake, physical activity, height, weight, employment status, familial status, previous number of visits and referrals to physicians. Participants were also asked to confirm whether the attending GP was their regular primary care physician or not. In France, all citizens are required to choose a GP as their regular physician. This study was based on patients who reported being seen exclusively by their regular family physician. Health-related quality of life was assessed using the validated 12-item Short Form (SF-12) questionnaire,[13] allowing estimation of physical health (PCS score) and mental health (MCS score); the SF-12 questionnaire was validated in the late 90s for use in the US, the UK, France and many other European countries.[14] Patients also completed the Complementary and Alternative Medicine Beliefs Inventory (CAMBI), which assesses attitudes and expectations of patients towards medical care, participation in decision making, perception of risks associated with treatment, and understanding of both illness and healing process via a 17-question inventory.[15] High scores on the CAMBI items indicate pro-CAM treatment belief. GPs recorded the main reason for consultation and up to five other diagnoses present that day as well as their prescriptions, which were entered by the interviewer in a database that automatically recorded the corresponding ATC (Anatomical Therapeutic Chemical) codes, revision 2009. Diagnoses relating to 100 diseases[2] were coded by a trained archivist using the 9th revision of the International Classification of Diseases.[16] Patients with the following ICD codes were classified as anxious: 300.0 anxiety states; 300.2 phobic disorders; 300.3 obsessive-compulsive disorders; 300.5 neurasthenia; 300.8 somatoform disorders; 306.2 psychogenic disease related to underlying physiological disorders. Patients with the following ICD codes were classified as depressive: 296.3

major depressive disorder, recurrent episode; 296.5 bipolar disorder, most recent episode depressed; 296.1 manic disorder; 296.6 manic-depressive psychosis; 300.4 dysthymic disorders; 300.5: neurasthenia; 309.0 adjustment reaction, 309.1 prolonged depressive reaction, 311.9 unclassified depressive disorders. Patients were considered as experiencing sleep disorders if their diagnoses related to ICD codes 307.4 (specific disorders of sleep of non-organic origin) and 780.5 (sleep disturbances).

Comorbidity was defined as the presence of at least one diagnosis other than the principal motive for consultation at the recruitment visit. Comorbidities were categorised as: co-associated sleep, anxiety, or depressive disorder (other than the main reason for consultation), musculoskeletal disorders, respiratory diseases, cardiovascular and metabolism disorders, diabetes, thyroid and endocrine disorders, and finally digestive disorders. Severity of SADD was characterised firstly by degree of quality of life (QoL) impairment, then by the presence and finally by number of associated comorbidities.

Statistical analysis

Characteristics of non-participants (age, gender, length of time attending the GP's medical practice, type of health insurance and main reasons for consultation) were used to calibrate the final sample as previously reported[2] to ensure that it would closely represent the whole population attending French GPs practices, using a method known in demographic studies as the CALMAR procedure.[17] Overall characteristics of patients seeking access to each of the three types of GP and results reported here were based on weighted data. Distributions were compared using Chi-Square and Fisher tests for categorical variables and Student and Wilcoxon tests for continuous variables.

Multiple logistic regression analyses were used to compare patients in the GP-Homeo and GP-Mixed groups to the GP-CM group for categorical variables and were adjusted for all variables listed in Table 1 to control for potential confounding.

Table 1. Characteristics of patients seeking care for SADD according to the type of practice of their regular GP (EPI3 Survey, n=1572)

	GP-CM (n=410) N, weighted %		GP-Mixed (n=718) N, weighted %		GP-Homeo (n=444) N, weighted %	
Gender						
Females vs. Males	269	64.7	500	68.9	323	72.6*
Age categories (years)						
18-39	92	20.7	195	26.7	131	28.8*
40-59	163	38.9	298	41.3	193	43.6*
60 and over	155	40.4	225	32.0	120	27.6*
Employment status						
Employed	171	39.5	353	48.9	240	53.5*
Educational level						
Secondary school /not completed	93	22.1	177	22.9	158	35.2*
Universal Health Insurance coverage (CMU)	36	9.5	65	9.8	26	6.5
Familial status						
Living with children	164	38.1	306	42.5	195	44.1*
Living with a spouse	239	56.6	439	61.2	285	64.0*
Body Mass Index (%)						
<25	216	52.1	413	57.9	302	67.9*
25-30	124	30.9	186	25.6	106	24.0*
>30	70	17.0	119	16.6	36	8.1*
Tobacco consumption (%)						
Never smoked	195	48.4	365	50.8	251	57.1*
Past smoker	111	26.9	170	23.6	112	24.6*
Current smoker	104	24.8	183	25.6	81	18.3*
Alcohol Consumption (%)						
Never	152	37.4	287	40.0	142	32.4
Sometimes	193	46.4	354	49.3	254	56.2
Daily	65	16.3	77	10.7	48	11.4
Physical exercise (%)						
31 minutes and over per day	125	30.7	207	29.3	140	31.6
Number of visits to regular GP during the last year						
None	7	1.7	16	2.3	10	2.2
1-6	228	55.4	405	57.0	296	66.8*
7-12	142	34.6	234	32.1	114	25.6*
12+	33	8.4	63	8.7	24	5.4*
Number of visits to a specialist during the last year						
None	105	25.8	200	28.0	113	25.6
1	114	27.0	206	28.6	137	31.2
2	63	15.6	133	18.4	82	18.1
2+	128	31.5	179	25.0	112	25.1
Motive for consultation (ICD-9)						
Anxiety	79	18.8	158	21.2	133	30.2*
Depression	171	41.1	284	39.6	127	28.7*
Sleep disorders	131	32.7	198	28.9	151	34.0
Unspecified	52	12.6	95	12.5	65	14.1
Treatment						

Any psychotropic drugs	266	64.0	404	55.4	138	31.2*
<i>Antidepressants</i>	152	36.0	231	31.5	73	16.5*
<i>Anxiolytics/hypnotics</i>	185	44.8	286	39.3	87	19.8*
<i>Antipsychotics</i>	11	3.1	25	3.5	10	2.4
<i>Normothymics</i>	16	3.9	7	1.1	20	4.6
Other conventional drugs	144	36.0	289	41.2	189	42.7
Homeopathic medicines for SADD	1	0.2	36	4.9	139	30.9*
Other homeopathic medicines	6	1.4	58	7.8	288	67.7*

Abbreviations: GP-CM (general practitioner using conventional medicine); GP-Mixed (general practitioner using mixed practice); GP-Homeo (general practitioner with a clear orientation towards homeopathic medicines)

*Difference with conventional medicine category statistically significant ($p \leq 0.05$) in logistic regression including all variables

The GP-Mixed and GP-Homeo groups were compared with the GP-CM group for patients' exposure to antidepressants (ATC codes beginning with N06AB, N06AX, N06AA and N06AF), anxiolytics and hypnotics (ATC codes beginning with N05BA, N05BB, N05BX, N05BE, N05CD, N05CF and N03AE) mood normalizers (N05AN, N03AG) and antipsychotics (ATC codes beginning with N05AK, N05AA, N05AB, N05AC, N05AD, N05AF, N05AG, N05AH, N05AL, N05AX, N07XX) as well as homeopathic preparations specifically prescribed for SADD symptoms.

ANCOVA analyses were performed to provide mean scores for the SF-12 mental (MCS) and physical scales (PCS) adjusted for age (<40, 40-60, 60+ years), gender, marital status, employment status, body mass index (BMI), number of associated comorbidities (other than SADD), and finally associated SADD (other than the main diagnose, yes/no). MCS score and PCS score were categorised into quartiles corresponding to: 34.1 (Q1), 42.4 (Q2), and 48 (Q3) for MCS; 39.3 (Q1), 47.3 (Q2) and 54.2 (Q3) for PCS.

Associations between scores from each of the 17 questions of the CAMBI questionnaire and the propensity to attend a GP-Mixed or GP-Homeo as compared to a GP-Allo were computed after adjusting for age, gender and educational level. Scores obtained per question, ranging from 1 (totally disagree) to 7 (totally agree), were dichotomised in order to further distinguish participants clearly in favour (scoring 5 to 7) or in disagreement (scoring 1 to 3) with the 17 CAMBI questions. Each of the three subscales scores and the total CAMBI score were then dichotomised according to the 75th percentile (40, 26 and 33, respectively; 96 for the total score).

The possibility of a clustering effect at the practice level was tested using Generalised Estimating Equations (GEE) multivariate models. All the analyses were performed with SAS software version 9.1 (SAS Institute, Inc., Cary, North Carolina).

The study was approved by the French National Data-Protection Commission (CNIL) and the French Medical Association (CNOM). Participating physicians received compensation fees for recruiting patients but not patients.

RESULTS

Among the 11 701 patients attending the doctor’s office on the surveyed day, 8559 (73.1%) accepted to participate in the survey and among these, 6379 indicated the consulting physician as their regular GP. A total of 1572 patients were included in the analysis because they were diagnosed by their family physician with anxiety (n=370), depression (n=583), and sleep disorders (n=480) or SADD of undetermined cause (n=139) according to the ICD classification.

Table 1 presents the characteristics of patients according to their GPs prescribing preferences (410 GP-CM, 718 GP-Mixed, and 444 GP-Homeo). Compared to the GP-CM group, patients from the GP-mixed group showed similar characteristics but those from the GP-Homeo group were more frequently younger, more educated, employed women living with children or a spouse. They also had a healthier lifestyle with lower BMI, and were more frequently non-smokers and occasional or non-consumers of alcohol.

Patients in the GP-Homeo group declared less visits to their regular GP in the previous year. Similar proportions of patients in the GP-CM and GP-Mixed groups consulted for anxiety (21.2 vs. 18.8%), depression (39.6 vs. 41.1%) or sleep disorders (28.9 vs. 32.7%). Patients were more likely to seek GP-Homeo for anxiety (30.2%) while less likely to consult them for depression than GP-CM (28.7%). No difference was found for depression between the two groups of GPs after adjustment for age.

Considering drug prescriptions, patients in the GP-CM group were more frequently prescribed psychotropic drugs for SADD (64.0%) than patients from the GP-Mixed (55.4%) and GP-Homeo group

(31.2%), the differences being statistically significant ($p < 0.001$). Among psychotropic drugs, antidepressants and anxiolytic-hypnotic drugs were less often prescribed in the GP-Homeo group (16.5% and 19.8%, respectively) as compared to GP-CM prescriptions (36.0% and 44.8%, respectively); these differences were statistically significant ($p < 0.001$). Antipsychotics and mood-stabilisers, which are usually prescribed for severe mental disorders (bipolar disorders and schizophrenia), were prescribed to similar proportions of patients in the three groups ($p = 0.44$ and $p = 0.09$, respectively).

A total of 30.4% and 15.6% of patients with SADD seeking care from GP-Mixed and GP-Homeo, respectively, received concomitantly a psychotropic and a homeopathic drug. Considering the severity of mental health problems, Table 2 shows that three quarters of patients with SADD exhibited at least one other comorbidity. No differences were observed between the three groups, with the exception of cardiovascular and metabolism disorders that were significantly more frequent in the GP-CM group (35.1%) as compared to GP-Homeo (22.9%). This difference was not statistically significant when adjusted for age and BMI of the patients.

Table 2. Burden of associated comorbidity and other psychological distress in patients with sleep, anxiety, or depressive disorders according to the type of practice of regular GPs (EPI3 Survey, $n = 1572$)

Comorbidities present at the medical visit	GP-CM Weighted%	GP-Mixed Weighted%	Gp-Homeo Weighted%
Patients with SADD ($n = 1572$)*	$n = 410$	$n = 718$	$n = 444$
Associated SADD comorbidity (other than primary)	7.4	2.6 ⁺	5.3
At least one other comorbidity	74.3	68.7	69.5
<i>MSD</i>	27.1	23.8	24.8
<i>Respiratory diseases</i>	16.6	11.7	18.5
<i>Cardiovascular and metabolism disorders</i>	35.1	30.2	22.9 ⁺
<i>Diabetes, thyroid and endocrine disorders</i>	12.7	9.6	8.1
<i>Digestive disorders</i>	11.9	11.5	11.5
Patients with depression ($n = 583$)	$n = 171$	$n = 285$	$n = 127$
Associated SADD comorbidity (other than depression)	13.7	3.7 ⁺	10.0
At least one other comorbidity	75.2	67.3 ⁺	70.6 ⁺
<i>MSD</i>	29.2	23.2	28.6
<i>Respiratory diseases</i>	15.3	9.8 ⁺	12.8
<i>Cardiovascular and metabolism disorders</i>	36.5	30.4	21.6 ⁺

<i>Diabetes, thyroid and endocrine disorders</i>	13.0	10.8	7.9 ⁺
<i>Digestive disorders</i>	10.4	9.0	10.6
Patients with anxiety (n=370)	n=79	n=158	n=133
Associated SADD comorbidity (other than anxiety)	12.9	5.7 ⁺	13.6
At least one other comorbidity	71.2	72.2	62.2 ⁺
<i>MSD</i>	22.5	26.5	25.2
<i>Respiratory diseases</i>	14.3	9.8	14.2
<i>Cardiovascular and metabolism disorders</i>	23.6	31.2 ⁺	22.3
<i>Diabetes, thyroid and endocrine disorders</i>	10.7	11.7	9.3
<i>Digestive disorders</i>	18.1	15.0	13.7
Patients with sleep disorder (n=480)	n=131	n=198	n=151
Associated SADD comorbidity (other than sleep disorder)	9.8	3.7	9.7
At least one other comorbidity	71.3	63.6	67.6
<i>MSD</i>	29.7	22.0	21.9 ⁺
<i>Respiratory diseases</i>	14.3	12.7	21.2
<i>CV and metabolism disorders</i>	37.8	28.9	19.4
<i>Diabetes, thyroid and endocrine disorders</i>	10.4	5.6 ⁺	4.4 ⁺
<i>Digestive disorders</i>	10.2	10.7	12.1

Abbreviations: GP-CM, general practitioner using conventional medicine; GP-Mixed, general practitioner using mixed practice; GP-Homeo, general practitioner with a clear orientation towards homeopathic medicines; MSD, musculoskeletal disorders; SADD: sleep, anxiety or depressive disorders

*Including missing diagnosis (according to ICD9) values (n=139 patients)

+Difference with conventional medicine category statistically significant ($p \leq 0.05$) in logistic regression including age (<40, 40-60, 60+ years), gender, marital status, employment status, BMI (body mass index: <25; 25-30; >30kg/m²), MCS: SF12-Mental Component Summary score; PCS: SF12-Physical Component Summary score.

For quality of life, the analysis of covariance showed that the mental score summary (MCS) of the SF-12 was similar across the three groups with no clinically or statistically meaningful differences (Table 3). For the physical summary score (PCS), higher values were found for each group of patients exhibiting at least one of the diseases and attending GP-Homeo. No differences in either PCS or MCS were found when comparing GP-Mixed to GP-CM.

Table 3. Adjusted quality of life (MCS and PCS) of patients visiting their regular GP according to the type of practice (EPI3 Survey, n=1572)

Quality of Life SF-12	GP-CM Mean (sd)*	GP-Mixed Mean (sd)*	p-value*	GP-Homeo Mean (sd)*	p-value*
SADD					
MCS	35.3 (1.0)	35.9 (1.0)	0.64	36.4 (1.0)	0.24
PCS	42.3 (1.0)	42.9 (1.0)	0.58	45.4 (1.0)	<0.001

Anxiety

MCS	36.7 (1.4)	35.8 (1.2)	0.73	37.3 (1.2)	0.88
PCS	44.1 (1.4)	44.8 (1.2)	0.81	47.4 (1.3)	0.03

Depression

MCS	34.5 (1.4)	34.6 (1.5)	0.99	34.0 (1.6)	0.92
PCS	40.5 (1.5)	41.9 (1.5)	0.29	44.1 (1.6)	0.006

Sleep disorders

MCS	34.6 (1.6)	37.0 (1.6)	0.06	35.7 (1.7)	0.64
PCS	44.4 (1.6)	44.3 (1.7)	0.99	47.5 (1.7)	0.03

Abbreviations: GP-CM, general practitioner using conventional medicine; GP-Mixed, general practitioner using mixed practice; GP-Homeo, general practitioner with a clear orientation towards homeopathic medicines; MSD, musculoskeletal disorders; MCS, SF12-mental component summary score; PCS: SF12-physical component summary score SADD: sleep, anxiety or depressive disorders

*from ANCOVA adjusted for age (<40, 40-60, 60+ years), gender, marital status, employment status, BMI, number of associated comorbidities (other than main SADD), SADD comorbidity (yes/no)

The attitudes towards complementary medicine estimated by CAMBI are shown in Table 4.

Somewhat similar attitudes and beliefs towards homeopathy and CAM were found between participants with SADD seeking care from GP-Mixed and GP-Allo, although a higher trust in natural treatment was observed in patients from GP-Mixed (OR = 1.15, 95% CI [1.03-1.26]). Three thirds of patients experiencing SADD from the GP-Homeo group, had an overall CAMBI score above 96 points (OR= 3.65, 95% CI [2.94-3.77]) as compared to participants consulting a GP-Allo. These results were consistent for each of the three subscales of the CAMBI, that is OR= 2.08, 95% CI [1.78-2.32], OR= 1.43, 95% CI [1.23-1.77], and OR= 2.75, 95% CI [2.55-3.24] for “natural” treatment, active participation of patients in the treatment process and holistic medicine, respectively.

Table 4. Attitudes of patients with SADD towards complementary medicine as measured by the CAMBI (attitudes towards complementary and alternative medicine beliefs inventory) questionnaire (EPI3 Survey, n=1572)

	Type of practice	
	GP-Mixed vs. GP-Allo OR* (95% CI)	GP-Homeo vs. GP-Allo OR* (95% CI)
1. Treatments should have no negative side effects	1.11 (0.94-1.33)	1.70 (1.43-1.93)
2. It is important to me that treatments are not	0.85 (0.65-1.14)	1.55 (1.41-2.03)

toxic		
3. Treatments should only use natural ingredients	1.07 (0.97-1.08)	2.02 (1.87-2.47)
4. It is important that treatments boost my immune system	1.12 (0.93-1.18)	1.65 (1.38-2.11)
5. Treatments should allow my body to heal itself	1.28 (1.13-1.38)	2.02 (1.77-2.18)
6. Treatments should increase my natural ability to keep healthy	1.05 (1.01-1.34)	1.54 (1.64-2.27)
7. Treatment providers should treat patients as equals	1.01 (0.89-1.17)	1.24 (1.08-1.67)
8. Patients should take an active role in their treatment	0.88 (0.81-1.06)	1.75 (1.18-1.81)
9. Treatment providers should make all decisions about treatment	0.85 (0.74-1.07)	1.37 (1.21-1.54)
10. Treatment providers should help patients make their own decisions about treatment	0.94 (0.86-1.11)	2.43 (1.89-2.43)
11. Treatment providers control what is discussed during consultations	1.04 (0.85-1.19)	1.37 (1.18-1.45)
12. Health is about harmonising your body, mind and spirit	1.08 (0.95-1.20)	2.33 (1.55-2.45)
13. Imbalances in people's lives are a major cause of illness	1.15 (1.02-1.27)	2.07 (1.66-2.07)
14. Treatments should focus only on symptoms rather than the whole person	0.82 (0.78-1.04)	2.44 (1.75-2.45)
15. Treatments should focus on people's overall well-being	1.21 (1.01-1.44)	1.53 (1.48-1.95)
16. I think my body has a natural ability to heal itself	1.13 (0.95-1.22)	2.43 (1.70-2.22)
17. There is no need for treatments to be associated to natural healing power	1.00 (0.77-1.07)	1.56 (1.33-1.81)
CAMBI Total score >Q3	1.05 (0.92-1.29)	3.65 (2.94-3.77)
CAMBI sub-scores:		
• Natural treatment >Q3	1.15 (1.03-1.26)	2.08 (1.78-2.32)
• Patient's participation >Q3	0.95 (0.81-1.03)	1.43 (1.23-1.77)
• Holistic medicine >Q3	1.15 (0.95-1.17)	2.75 (2.55-3.24)

Abbreviations: CI,: confidence interval; GP-Allo, GP practising conventional medicine; GP-Homeo, GP practising homeopathy; GP-Mixed, GP using mixed practice; OR, odds-ratio
*adjusted for age, gender and educational level.

DISCUSSION

To our knowledge, the EPI3 study is the first nationwide survey conducted in a large representative sample of patients to provide characteristics and attitudes, as well as the first to quantify quality of life and the burden of sleep, anxiety or depressive disorders (SADD) in patients seeking care from their regular GPs with different prescribing preferences towards CAM and homeopathic medicines. Our results suggest that patients experiencing SADD, and who chose a GP with a clear orientation towards homeopathy, differed in their socio-demographic profile but not in the severity of their mental illness from those attending regular GPs with prescribing preferences towards conventional psychotropic drugs. Patients with SADD attending a GP-Homeo in our study were more likely to be female, as previously reported[18-21] except for one survey,[22] and younger; age as also been suggested by other authors,[23] although no such association has been described elsewhere.[18,20,22] They also had healthier lifestyle habits as shown by low BMI and non-smoking habits; also noteworthy is the higher educational attainment found among patients seeking mixed and homeopathic GPs, which has been also previously reported in some[18,20] but not all related studies.[21,22] More educated people may be more knowledgeable about the side effects of conventional psychotropic drugs and hence more likely to seek alternative treatments as suggested by Mac Lennan et al.[19]

With regard to the medical conditions, the EPI3 survey is one the few studies highlighting that sleep, anxiety and depressive disorders show similar burdens in terms of severity and impact on mental impairment regardless of practice modalities of GPs. As for prevalence, anxiety was confirmed as the most frequent mental health disorder encountered by alternative medicine practitioners, as previously reported.[5,11] Higher prevalence of patients suffering from depression seeking GP-CM might be attributed to the older age structure observed in this group when compared to those consulting GP-Homeo: age trajectories observed for depression are often the opposite as those found for anxiety.[24] In spite of the fact that patients with depressive disorders in our study were less likely to seek strict homeopaths than GP-CM, we must remember that depression is also one of

the most commonly treated complaints as previously described for outpatient clinics of homeopathic hospitals in the UK National Health Service.[25]

Studies examining representative samples of general population seeking care for SADD have consistently shown that a large proportion of subjects are not treated with psychotropic drugs.^{26,27} Conversely, psychotropic drugs use is frequently reported by subjects without identified psychiatric disorders.[28] This latter observation is probably the reason why there is an increasing trend for patients falling into the mixed category with similar characteristics and SADD: as if they sought a combination of both homeopathy and CM to fulfil individualised and holistic therapies needs and expectations, whilst being sure that good standards of medical and scientific practice were met.[29] This type of patient seems to be primarily concerned by associating their need for care and adequate treatment. The CAMBI scores (related to trust and beliefs in CAM) were found to be strongly associated to participants from the GP-Homeo group, but also modestly to the GP-Mixed group. One third of the patients with SADD consulting a GP-Mixed received concomitantly homeopathic medicines and a psychotropic drug: this might suggest that homeopathic medicines could be prescribed not only as a substitute of unnecessary conventional psychotropic drugs, but also viewed as an adjunct to efficient psychotropic drugs;[11,21,30] such combination has been found to potentially help patients to accept and improve their symptoms[31] whilst avoiding some possible side effects of additional conventional therapies. Although no conclusions can be drawn at this stage on the outcome of consultations to GP-Mixed and GP-Homeo and whether their patients were given adequate treatment, our study highlights a genuine will from GP-Mixed and GP-Homeo to tailor therapies to their patients while avoiding unnecessary prescriptions.

Remarkably and regardless their mental health problems, patients scored similar adjusted mental severity for mental health diseases across the different groups of GPs and were diagnosed a somewhat similar number of comorbidities at the medical practice. Some studies found that patients seeking CAM therapies showed more QoL impairment than patients seeking conventional therapies.[32] Other studies, including ours, suggest that, despite the modality of practice (CAM or

conventional therapies), GPs treat patients exhibiting similar mental health problems and disease burden.[33]

Around 75% of patients who sought GPs exhibited additional morbidities in the EPI3 survey. The role of comorbidity in producing further burden from sleep, anxiety and depressive disorders has not been studied in patients attending GPs practising different modalities of treatment.[34,35]

Integrating research to understand the role of comorbidity in QoL is challenging due to differences across studies in QoL conceptualisation, validity of QoL measurement, recruitment context (e.g., epidemiological, treatment-seeking), and consideration of socio-demographic and clinical predictors. Studies generally account for a limited range of comorbidity attributes, typically the presence versus absence of comorbidity, which loses the richness of information inherent in psychiatric presentations.

Together with a lower number of visits to GPs and a lower proportion of prescribed psychotropic drugs in the GP-Homeo group, our findings may have relevant public health implications. For instance, the National Institute for Health and Clinical Excellence (NICE), highlighted recently that the severity of depression at which antidepressants show consistent benefits over placebo is poorly defined, emphasising that, in general, the more severe the symptoms, the greater the benefit.[36] A patient-level meta-analysis demonstrated a lack of efficacy for antidepressants in the majority of patients with anxiety and depressive disorders.[3,4] Thus, the real impact of conventional antidepressants in this population is considerable, with adverse reactions outweighing potential benefits.[37] The patient's dissatisfaction with psychotropic drugs is one of the reasons cited for seeking other treatment options[38] and patients with a history of depression are more likely to seek CAM than those who have never been depressed before.[39]

Under a primary care system designed for acute rather than chronic care, where clinicians "routinely experience the tyranny of the urgent", [40] our results suggested that management of SADD by GP-Homeo was associated with less visits to the GP in the previous year but no more consultations to specialists than GP-CM. Medico-economic studies are needed to assess the patterns of access to and

management by these different practitioners, which would contribute to better plan resource allocation for mental health services and target key groups for interventions in prevention, as far as severity of SADD is concerned.

Strengths and limitations of the study

The present study examined a relatively large number of primary care practices in order to provide a real-world picture of CAM and homeopathic practice within the French primary care setting. The main strengths of the EPI3 survey have already been acknowledged elsewhere.[2] These include high representativeness of the patients involved and comparability against other nationwide studies. The weighted geographical distribution of the participating GPs in the survey was similar to the national distribution of GPs in private practice across the 22 French regions surveyed, and the distribution of physicians’ individual characteristics regarding age, gender, type of contract with national health insurance and modality of practice differed only slightly from national statistics.[2]

The main limitation of our study relates to the classification of GPs, which relied on self-reporting of CAM prescriptions. The definition of GP-Homeo was more accurate and based on their professional certification. Therefore, generalisations of the results must be made cautiously, since our findings represented general practice in France. Nevertheless, this particular setting can be otherwise interpreted also as a strength, because it provided a unique opportunity to compare head-to-head primary care practices differing only by preferences for homeopathy and CAM, whereas all participant physicians shared similar medical professional status and basic training in conventional medicine. We feel that albeit the context of the study was specific to one country, differences between the groups of patients provided reliable information on the differential utilisation of homeopathy and CAM.

Finally, the fact that the participants were recruited in primary care might have excluded people with severe psychiatric disorders. This potential bias was likely to underestimate the prevalence of psychotropic drug use. However, prescriptions for psychotropic drugs were similar to those found in other French studies.[42,43]

CONCLUSION

The EPI3 survey is one of the largest studies to date conducted in general practice to assess the determinants, attitudes and burden of sleep, anxiety and depressive disorders in patients seeking care from GPs with different prescribing preferences towards CAM and homeopathic medicines. Our results showed that patients with SADD, while differing principally in their socio-demographic profiles and conventional psychotropic prescriptions, were actually rather similar regarding the severity of SADD in terms of comorbidities and QOL. Further research is needed to explore potential benefits, both in terms of health economics and care, of consulting GPs that combine CAM and CM daily in the clinical management of SADD.

1
2
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14 **Competing interests**
15

16
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31
32 **Contributors**
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34
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36
37 DG, BA, GD, A-MM, MR and LA conceived both the research theme and the methods, analysed the
38
39 data and interpreted the results. LG-B implemented the trial in France, analysed the data, and
40
41 together with FL, PE and LA drafted and revised the paper. All members of the EPI3-LA-SER group
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43 designed the study. A Fabre and PE analysed the data. All authors have contributed to, read and
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46
47 of the data in the study and take responsibility for the integrity of the data and the accuracy of the
48
49 data analysis.
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54 **Data sharing statement**
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Who seeks primary care for sleep, anxiety and depressive disorders from physicians prescribing homeopathic and other complementary medicine? Results from the EPI3 population survey.



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Who seeks primary care for sleep, anxiety and depressive disorders from physicians prescribing homeopathic and other complementary medicine? Results from the EPI3 population survey.

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1
2
3 **Abstract**
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7 **Objectives:** To describe and compare patients seeking treatment for sleep, anxiety and depressive
8 disorders (SADD) from physicians in general practice (GPs) with three different practice preferences:
9 strictly conventional medicine (GP-CM), mixed complementary and conventional medicine (GP-Mx),
10 and certified homeopathic physicians (GP-Ho).
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15 **Design and setting:** The EPI3 survey was a nationwide, observational study of a representative
16 sample of general practitioners and their patients, conducted in France between March 2007 and
17 July 2008.
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21 **Participants:** 1572 patients diagnosed with SADD.
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24 **Primary and secondary outcomes:** Patients' attitude towards complementary and alternative
25 medicine (CAM); psychotropic drug utilisation.
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27

28 **Results:** Compared to patients attending GP-CM, GP-Ho patients had healthier lifestyles whilst GP-
29 Mx patients showed similar profiles. Psychotropic drugs were more likely to be prescribed by GP-CM
30 (64%) than GP-Mx (55.4%) and GP-Ho (31.2%). The three groups of patients shared similar SADD
31 severity.
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34
35

36 **Conclusion:** Our results showed that patients with SADD, whilst differing principally in their socio-
37 demographic profiles and conventional psychotropic prescriptions, were actually rather similar
38 regarding the severity of SADD in terms of comorbidities and QOL. This information may help to
39 better plan resource allocation and management of these common health problems in primary care.
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48 **Article summary**
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51 **Article focus**
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- 53 • Up to 20% of patients attending primary healthcare in developed countries suffer from the
54 often linked anxiety and depression disorders.
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- Conventional treatments, particularly antidepressants and anxiolytics, are widely prescribed; often associated with adverse side effects, conventional treatments are a likely cause for an increasing number of patients to choose homeopathy and other complementary therapies.
- Understanding the characteristics of physicians and patients, prescribing or using homeopathy, respectively, in conjunction with or instead of psychotropic drugs is undoubtedly of clinical and public health relevance.

Key messages

- Our results suggest that patients experiencing SADD who chose a GP with a clear orientation towards homeopathy, differed in their socio-demographic profile but not in the severity of their mental illness from those attending regular GPs with prescribing preferences towards conventional psychotropic drugs.
- Our survey is one the few studies highlighting that sleep, anxiety and depressive disorders show similar burdens in terms of severity and impact on mental impairment regardless of GPs' prescribing preferences.
- Our results showed that patients with SADD, whilst differing principally in their socio-demographic profiles and conventional psychotropic prescriptions, were actually rather similar regarding the severity of SADD in terms of comorbidities and QOL

Strengths and limitations

- Strengths of the EPI-3 study include high representativeness of the patients involved and comparability against other nationwide studies.
- The main limitation of our study relates to the classification of GPs, which relied on self-reporting of complementary and alternative medicine (CAM) prescriptions; generalisations of the results must be therefore made cautiously since our findings relate to general practice in France.

INTRODUCTION

Mental health problems such as sleep, anxiety or depressive disorders (SADD) are responsible for considerable disability worldwide[1] resulting in serious quality of life impairment[2] and are often associated with high use of medical services. It is estimated that up to 20 percent of patients attending primary healthcare in developed countries suffer from the often linked disorders of anxiety and depression. A high prescription rate of conventional therapies, particularly antidepressants,[3,4] which are often associated with adverse side effects, are a likely cause for an increasing number of patients to choose homeopathy and other complementary therapies.[5]

Evidence of effectiveness of these therapies compared to conventional psychotropic drugs is still limited.[6-8] Nonetheless, their perceived safety may be an important factor motivating patients with SADD disorders to seek care from GPs preferring homeopathy and other types of complementary medicine. Among complementary alternative medicine (CAM) modalities of practice, homeopathy is widely used in countries with large access to conventional medicine and represents a particularly good marker for CAM practice in France, where homeopathic drugs are partly reimbursed by national health insurance and prescribed only by a medical practitioner, if not purchased as over-the-counter drugs.[9] In a previous study,[10] homeopathic practitioners (including non-medical healthcare professionals) indicated that their patients used homeopathy mainly in association with conventional psychotropic treatments, psychotherapy and counselling in a mixed practice.

Understanding the characteristics of physicians and patients, prescribing or using homeopathy, respectively, in conjunction with or instead of psychotropic drugs is undoubtedly of clinical and public health relevance. The objective of this study was to describe and compare patients seeking treatment for sleep, anxiety and depressive disorders (SADD) from physicians in general practice

(GPs) with three different practice preferences: strictly conventional medicine (GP-CM), mixed complementary and conventional medicine (GP-Mx), and certified homeopathic physicians (GP-Ho).

METHODS

Study design, settings and participants

The EPI3 survey was a nationwide, observational study of a representative sample of general practitioners and their patients, conducted in France between March 2007 and July 2008. The methodology of the study has been described elsewhere.[2]

Participants (GPs and their patients) were drawn by applying a two-stage sampling process. The GPs were first randomly selected from the French national directory of physicians and invited to participate, which meant allowing a research assistant to conduct a one-day survey in the waiting room at the doctor's practice. Blind to the study focus on conventional and complementary alternative medicine (CAM) practice, consenting GPs were next contacted by telephone to enquire how frequently they prescribed CAM (homeopathy, mesotherapy, acupuncture, phytotherapy, etc.). Depending on their prescribing preferences towards homeopathic medicines, they were classified as: strictly conventional GPs (GP-CM), who declared themselves never or rarely using CAM or homeopathic medicines; mixed practice (GP-Mx), who were GPs declaring using CAM regularly; and GPs certified in homeopathic practice (GP-Ho). In France, homeopathy can only be prescribed by physicians, mostly GPs qualified as homeopaths by the French National Council of Physicians (CNOM) upon completion of specific training and certification (3.3% of all French GPs in 2008).[11]

The second stage of selection consisted of random one-day sampling of consultations per participating physician, in order to survey all patients attending the practice on that very day. All adults (18 years old and over) and accompanied minor patients were eligible for inclusion in the EPI3 survey, except those whose health status or literacy level did not allow responding to a self-administered questionnaire.

During the consultation, GPs asked all adult patients diagnosed or suspected of suffering SADD whether they would volunteer for a more in-depth study of their disease. Consenting patients were contacted again within 72 hours for a telephone interview conducted by trained interviewers.

Data collection

Collection of data from patients included: age, gender, nationality, educational attainment, type of health insurance, additional private insurance, smoking habit, alcohol intake, physical activity, height, weight, employment status, familial status, previous number of visits and referrals to physicians. Participants were also asked to confirm whether the attending GP was their regular primary care physician or not. In France, all citizens are required to choose a GP as their regular physician. This study was based on patients who reported being seen exclusively by their regular family physician. Health-related quality of life was assessed using the validated 12-item Short Form (SF-12) questionnaire,[12] allowing estimation of physical health (PCS score) and mental health (MCS score); the SF-12 questionnaire was validated in the late 90s for use in the US, the UK, France and many other European countries.[13] Patients also completed the Complementary and Alternative Medicine Beliefs Inventory (CAMBI), which assesses attitudes and expectations of patients towards medical care, participation in decision making, perception of risks associated with treatment, and understanding of both illness and healing process via a 17-question inventory.[14] High scores on the CAMBI items indicate pro-CAM treatment belief. GPs recorded the main reason for consultation and up to five other diagnoses present that day as well as their prescriptions, which were entered by the interviewer in a database that automatically recorded the corresponding ATC (Anatomical Therapeutic Chemical) codes, revision 2009. Diagnoses relating to 100 diseases[2] were coded by a trained archivist using the 9th revision of the International Classification of Diseases.[15] Patients with the following ICD codes were classified as anxious: 300.0 anxiety states; 300.2 phobic disorders; 300.3 obsessive-compulsive disorders; 300.5 neurasthenia; 300.8 somatoform disorders; 306.2 psychogenic disease related to underlying physiological disorders. Patients with the following ICD codes were classified as depressive: 296.3

major depressive disorder, recurrent episode; 296.5 bipolar disorder, most recent episode depressed; 296.1 manic disorder; 296.6 manic-depressive psychosis; 300.4 dysthymic disorders; 300.5: neurasthenia; 309.0 adjustment reaction, 309.1 prolonged depressive reaction, 311.9 unclassified depressive disorders. Patients were considered as experiencing sleep disorders if their diagnoses related to ICD codes 307.4 (specific disorders of sleep of non-organic origin) and 780.5 (sleep disturbances).

Comorbidity was defined as the presence of at least one diagnosis other than the principal motive for consultation at the recruitment visit. Comorbidities were categorised as: co-associated sleep, anxiety, or depressive disorder (other than the main reason for consultation), musculoskeletal disorders, respiratory diseases, cardiovascular and metabolism disorders, diabetes, thyroid and endocrine disorders, and finally digestive disorders. Severity of SADD was characterised firstly by degree of quality of life (QoL) impairment, then by the presence and finally by number of associated comorbidities.

Statistical analysis

Characteristics of non-participants (age, gender, length of time attending the GP's medical practice, type of health insurance and main reasons for consultation) were used to calibrate the final sample as previously reported[2] to ensure that it would closely represent the whole population attending French GPs practices, using a method known in demographic studies as the CALMAR procedure.[16] Overall characteristics of patients seeking access to each of the three types of GP and results reported here were based on weighted data. Distributions were compared using Chi-Square and Fisher tests for categorical variables and Student and Wilcoxon tests for continuous variables.

Multiple logistic regression analyses were used to compare patients in the GP-CM group to GP-Mx and GP-Ho groups for categorical variables and were adjusted for all variables listed in Table 1 to control for potential confounding.

The GP-Mx and GP-Ho groups were compared to the GP-CM group for patients' exposure to antidepressants (ATC codes beginning with N06AB, N06AX, N06AA and N06AF), anxiolytics and hypnotics (ATC codes beginning with N05BA, N05BB, N05BX, N05BE, N05CD, N05CF and N03AE) mood normalisers (N05AN, N03AG) and antipsychotics (ATC codes beginning with N05AK, N05AA, N05AB, N05AC, N05AD, N05AF, N05AG, N05AH, N05AL, N05AX, N07XX) as well as homeopathic preparations specifically prescribed for SADD symptoms.

ANCOVA analyses were performed to provide mean scores for the SF-12 mental (MCS) and physical scales (PCS) adjusted for age (<40, 40-60, 60+ years), gender, marital status, employment status, body mass index (BMI), number of associated comorbidities (other than SADD), and finally associated SADD (other than the main diagnose, yes/no). MCS score and PCS score were categorised into quartiles corresponding to: 34.1 (Q1), 42.4 (Q2), and 48 (Q3) for MCS; 39.3 (Q1), 47.3 (Q2) and 54.2 (Q3) for PCS.

Associations between scores from each of the 17 questions of the CAMBI questionnaire and the probability of attending a GP-Mx or GP-Ho as compared to a GP-CM were computed after adjusting for age, gender and educational level. Scores obtained per question, ranging from 1 (totally disagree) to 7 (totally agree), were dichotomised in order to further distinguish participants clearly in favour (scoring 5 to 7) or in disagreement (scoring 1 to 3) with the 17 CAMBI questions. Each of the three subscales scores and the total CAMBI score were then dichotomised according to the 75th percentile (40, 26 and 33, respectively; 96 for the total score).

The possibility of a clustering effect at the practice level was tested using Generalised Estimating Equations (GEE) multivariate models. All the analyses were performed with SAS software version 9.1 (SAS Institute, Inc., Cary, North Carolina).

The study was approved by the French National Data-Protection Commission (CNIL) and the CNOM. Participating physicians received compensation fees for recruiting patients but not patients.

RESULTS

A total of 825 GPs participated in the survey. There was no difference between the three groups of GPs for age (mean = 50.7 years) but GP-Ho and GP-Mx were more often women than GP-CM (48.9% and 31.5% versus 20.3%, respectively), and less often salaried (14.3% and 16.9% versus 34.5%, respectively). In addition, GP-Ho were more likely to practise alone than GP-CM and GP-Mx (72.4% versus 51.8% and 55.9%, respectively) (all differences statistically significant). Among the 11 701 patients attending the doctor's office on the survey day, 8652 (73.9%) agreed to participate and complete information was collected for 8559 (73.1%) patients. Compared to non-participants, participants were more often women (62.7% and 56.8%, respectively), younger (mean age 43.3 and 47.7, respectively) and more likely to consult for a SADD (20.6% and 11.6%, respectively). Of the 6379 who declared the consulting physician as their regular GP, 1572 met the inclusion criteria and were included in the analyses with the following diagnoses: anxiety (n=370), depression (n=583), sleep disorders (n=480) or SADD of undetermined cause (n=139).

Compared to the GP-CM group, patients from the GP-Mx group showed similar characteristics but those from the GP-Ho group were more frequently younger, more educated, employed women living with children or a spouse (Table 1). They also had a healthier lifestyle with lower BMI, and were more frequently non-smokers and occasional or non-consumers of alcohol. They declared however less visits to their regular GP in the previous year. Motives of consultation showed more anxiety and less depression in the GP-Ho group than in the two others but the distribution was unremarkable otherwise. Physicians prescribing preferences were confirmed with the GP-Ho group using more homeopathy and less psychotropic drugs than the two other groups. The GP-Mx group however did not differ much from the GP-CM group.

Table 1. Characteristics of patients seeking care for SADD according to the type of practice of their regular GP (EPI3 Survey, n=1572)

	GP-CM (n=410)	GP-Mx (n=718)	GP-Ho (n=444)
	N, weighted %	N, weighted %	N, weighted %

Gender						
Females vs. Males	269	64.7	500	68.9	323	72.6*
Age categories (years)						
18-39	92	20.7	195	26.7	131	28.8*
40-59	163	38.9	298	41.3	193	43.6*
60 and over	155	40.4	225	32.0	120	27.6*
Employment status						
Employed	171	39.5	353	48.9	240	53.5*
Educational level						
Secondary school not completed	93	22.1	177	22.9	158	35.2*
Universal Health Insurance coverage (CMU)						
	36	9.5	65	9.8	26	6.5
Familial status						
Living with children	164	38.1	306	42.5	195	44.1*
Living with a spouse	239	56.6	439	61.2	285	64.0*
Body Mass Index (%)						
<25	216	52.1	413	57.9	302	67.9*
25-30	124	30.9	186	25.6	106	24.0*
>30	70	17.0	119	16.6	36	8.1*
Tobacco consumption (%)						
Never smoked	195	48.4	365	50.8	251	57.1*
Past smoker	111	26.9	170	23.6	112	24.6*
Current smoker	104	24.8	183	25.6	81	18.3*
Alcohol Consumption (%)						
Never	152	37.4	287	40.0	142	32.4
Sometimes	193	46.4	354	49.3	254	56.2
Daily	65	16.3	77	10.7	48	11.4
Physical exercise (%)						
> 30 minutes / day	125	30.7	207	29.3	140	31.6
Number of visits to regular GP during the last year						
None	7	1.7	16	2.3	10	2.2
1-6	228	55.4	405	57.0	296	66.8*
7-12	142	34.6	234	32.1	114	25.6*
12 and over	33	8.4	63	8.7	24	5.4*
Number of visits to a specialist during the last year						
None	105	25.8	200	28.0	113	25.6
1	114	27.0	206	28.6	137	31.2
2	63	15.6	133	18.4	82	18.1
2+	128	31.5	179	25.0	112	25.1
Motive for consultation (ICD-9)						
Anxiety	79	18.8	158	21.2	133	30.2*
Depression	171	41.1	284	39.6	127	28.7*
Sleep disorders	131	32.7	198	28.9	151	34.0
Unspecified	52	12.6	95	12.5	65	14.1
Treatment						
Any psychotropic drugs	266	64.0	404	55.4	138	31.2*
<i>Antidepressants</i>	152	36.0	231	31.5	73	16.5*
<i>Anxiolytics/hypnotics</i>	185	44.8	286	39.3	87	19.8*
<i>Antipsychotics</i>	11	3.1	25	3.5	10	2.4
<i>Normothymics</i>	16	3.9	7	1.1	20	4.6
Other conventional drugs	144	36.0	289	41.2	189	42.7
Homeopathic medicines for SADD	1	0.2	36	4.9	139	30.9*
Other homeopathic medicines	6	1.4	58	7.8	288	67.7*

Abbreviations: GP-CM: general practitioner strictly practising conventional medicine; GP-Mx: general practitioner with mixed practice; GP-Ho: general practitioner with a certification in homeopathic care.

*Difference with conventional medicine category statistically significant ($p \leq 0.05$) in logistic regression including all variables.

Considering the severity of mental health problem, the GP-Mx group had systematically less often an associated SADD comorbidity than in the two other groups but the distribution of comorbidities other than SADD was unremarkable otherwise between groups (Table 2). For quality of life, the mental score summary (MCS) of the SF-12 was similar across the three groups with no clinically or statistically meaningful difference (Table 3). The GP-Ho group however had a slightly better physical summary score (PCS) than the two other groups.

Table 2. Burden of associated comorbidity and other psychological distress in patients with sleep, anxiety, or depressive disorders according to the type of practice of regular GPs (EPI3 Survey, n=1572)

Comorbidities present at the medical visit	GP-CM Weighted%	GP-Mx Weighted%	Gp-Ho Weighted%
Patients with SADD (n=1572)*	n=410	n=718	n=444
Associated SADD comorbidity (other than primary)	7.4	2.6 ⁺	5.3
At least one other comorbidity	74.3	68.7	69.5
MSD	27.1	23.8	24.8
Respiratory diseases	16.6	11.7	18.5
Cardiovascular and metabolism disorders	35.1	30.2	22.9 ⁺
Diabetes, thyroid and endocrine disorders	12.7	9.6	8.1
Digestive disorders	11.9	11.5	11.5
Patients with depression (n=583)	n=171	n=285	n=127
Associated SADD comorbidity (other than depression)	13.7	3.7 ⁺	10.0
At least one other comorbidity	75.2	67.3 ⁺	70.6 ⁺
MSD	29.2	23.2	28.6
Respiratory diseases	15.3	9.8 ⁺	12.8
Cardiovascular and metabolism disorders	36.5	30.4	21.6 ⁺
Diabetes, thyroid and endocrine disorders	13.0	10.8	7.9 ⁺
Digestive disorders	10.4	9.0	10.6
Patients with anxiety (n=370)	n=79	n=158	n=133
Associated SADD comorbidity (other than anxiety)	12.9	5.7 ⁺	13.6
At least one other comorbidity	71.2	72.2	62.2 ⁺
MSD	22.5	26.5	25.2
Respiratory diseases	14.3	9.8	14.2
Cardiovascular and metabolism disorders	23.6	31.2 ⁺	22.3

<i>Diabetes, thyroid and endocrine disorders</i>	10.7	11.7	9.3
<i>Digestive disorders</i>	18.1	15.0	13.7
Patients with sleep disorder (n=480)	n=131	n=198	n=151
Associated SADD comorbidity (other than sleep disorder)	9.8	3.7	9.7
At least one other comorbidity	71.3	63.6	67.6
<i>MSD</i>	29.7	22.0	21.9 ⁺
<i>Respiratory diseases</i>	14.3	12.7	21.2
<i>CV and metabolism disorders</i>	37.8	28.9	19.4
<i>Diabetes, thyroid and endocrine disorders</i>	10.4	5.6 ⁺	4.4 ⁺
<i>Digestive disorders</i>	10.2	10.7	12.1

Abbreviations: GP-CM: general practitioner strictly practising conventional medicine; GP-Mx: general practitioner with mixed practice; GP-Ho: general practitioner with a certification in homeopathic care; MSD: musculoskeletal disorders; SADD: sleep, anxiety or depressive disorders.

*Including missing diagnosis (according to ICD9) values (n=139 patients).

+Difference with conventional medicine category statistically significant ($p \leq 0.05$) in logistic regression including age (<40, 40-60, 60+ years), gender, marital status, employment status, BMI (body mass index: <25; 25-30; >30kg/m²), MCS: SF12-Mental Component Summary score; PCS: SF12-Physical Component Summary score.

Table 3. Adjusted quality of life (MCS and PCS) of patients visiting their regular GP according to the type of practice (EPI3 Survey, n=1572)

Quality of Life SF-12		GP-CM Mean (sd)*	GP-Mx Mean (sd)*	p-value*	GP-Ho Mean (sd)*	p-value*
SADD						
	MCS	35.3 (1.0)	35.9 (1.0)	0.64	36.4 (1.0)	0.24
	PCS	42.3 (1.0)	42.9 (1.0)	0.58	45.4 (1.0)	<0.001
Anxiety						
	MCS	36.7 (1.4)	35.8 (1.2)	0.73	37.3 (1.2)	0.88
	PCS	44.1 (1.4)	44.8 (1.2)	0.81	47.4 (1.3)	0.03
Depression						
	MCS	34.5 (1.4)	34.6 (1.5)	0.99	34.0 (1.6)	0.92
	PCS	40.5 (1.5)	41.9 (1.5)	0.29	44.1 (1.6)	0.006
Sleep disorders						
	MCS	34.6 (1.6)	37.0 (1.6)	0.06	35.7 (1.7)	0.64
	PCS	44.4 (1.6)	44.3 (1.7)	0.99	47.5 (1.7)	0.03

Abbreviations: GP-CM: general practitioner strictly practising conventional medicine; GP-Mx: general practitioner with mixed practice; GP-Ho: general practitioner with a certification in homeopathic care; MSD: musculoskeletal disorders; MCS: SF12-mental component summary score; PCS: SF12-physical component summary score SADD: sleep, anxiety or depressive disorders.

*from ANCOVA adjusted for age (<40, 40-60, 60+ years), gender, marital status, employment status, BMI, number of associated comorbidities (other than main SADD), SADD comorbidity (yes/no); a higher score indicates better health.

The attitudes towards complementary medicine estimated by CAMBI (Table 4) showed that patients in the GP-Ho group had a probability of scoring high (favourable to CAM) over three times that of the GP-CM group (Odds ratio (OR) = 3.65, 95% confidence interval (CI): 2.94-3.77). The result was consistent for each of the three CAMBI subscales with OR= 2.08 (95% CI: 1.78-2.32) for belief in natural treatment, OR= 1.43 (95% CI: 1.23-1.77) for active patient's participation in care, and OR= 2.75 (95% CI: 2.55-3.24) belief in holistic medicine. CAMBI scores from patients of the GP-Mx group were comparable to the GP-CM group, although a slightly higher trust in natural treatment subscale was observed (OR = 1.15, 95% CI: 1.03-1.26).

Table 4. Attitudes of patients with SADD towards complementary medicine as measured by the CAMBI (attitudes towards complementary and alternative medicine beliefs inventory) questionnaire (EPI3 Survey, n=1572)

	Type of practice	
	GP-Mx vs. GP-CM OR* (95% CI)	GP-Ho vs. GP-CM OR* (95% CI)
1. Treatments should have no negative side effects	1.11 (0.94-1.33)	1.70 (1.43-1.93)
2. It is important to me that treatments are not toxic	0.85 (0.65-1.14)	1.55 (1.41-2.03)
3. Treatments should only use natural ingredients	1.07 (0.97-1.08)	2.02 (1.87-2.47)
4. It is important that treatments boost my immune system	1.12 (0.93-1.18)	1.65 (1.38-2.11)
5. Treatments should allow my body to heal itself	1.28 (1.13-1.38)	2.02 (1.77-2.18)
6. Treatments should increase my natural ability to keep healthy	1.05 (1.01-1.34)	1.54 (1.64-2.27)
7. Treatment providers should treat patients as equals	1.01 (0.89-1.17)	1.24 (1.08-1.67)
8. Patients should take an active role in their treatment	0.88 (0.81-1.06)	1.75 (1.18-1.81)
9. Treatment providers should make all decisions about treatment	0.85 (0.74-1.07)	1.37 (1.21-1.54)
10. Treatment providers should help patients make their own decisions about treatment	0.94 (0.86-1.11)	2.43 (1.89-2.43)
11. Treatment providers control what is discussed during consultations	1.04 (0.85-1.19)	1.37 (1.18-1.45)
12. Health is about harmonising your body, mind and spirit	1.08 (0.95-1.20)	2.33 (1.55-2.45)
13. Imbalances in people's lives are a major cause of illness	1.15 (1.02-1.27)	2.07 (1.66-2.07)

14. Treatments should focus only on symptoms rather than the whole person	0.82 (0.78-1.04)	2.44 (1.75-2.45)
15. Treatments should focus on people’s overall well-being	1.21 (1.01-1.44)	1.53 (1.48-1.95)
16. I think my body has a natural ability to heal itself	1.13 (0.95-1.22)	2.43 (1.70-2.22)
17. There is no need for treatments to be associated to natural healing power	1.00 (0.77-1.07)	1.56 (1.33-1.81)
CAMBI Total score >Q3	1.05 (0.92-1.29)	3.65 (2.94-3.77)
CAMBI sub-scores:		
• Natural treatment >Q3	1.15 (1.03-1.26)	2.08 (1.78-2.32)
• Patient’s participation >Q3	0.95 (0.81-1.03)	1.43 (1.23-1.77)
• Holistic medicine >Q3	1.15 (0.95-1.17)	2.75 (2.55-3.24)

Abbreviations: GP-CM: general practitioner strictly practising conventional medicine; GP-Mx: general practitioner with mixed practice; GP-Ho: general practitioner with a certification in homeopathic care; OR: Odds ratio

*adjusted for age, gender and educational level.

DISCUSSION

To our knowledge, the EPI3 study is the first nationwide survey conducted in a large representative sample of patients to provide characteristics and attitudes, as well as the first to quantify quality of life and the burden of sleep, anxiety or depressive disorders (SADD) in patients seeking care from their regular GPs with different preferences towards CAM and homeopathic practices.

Our results suggest that patients experiencing SADD, and who chose a GP with a clear orientation towards homeopathy, differed in their socio-demographic profile but not in the severity of their mental illness from those attending regular GPs with prescribing preferences towards conventional psychotropic drugs. Patients with SADD attending a GP-Ho in our study were more likely to be female, as previously reported[17-20] except for one survey,[21] and younger; age as also been suggested by other authors,[22] although no such association has been described elsewhere.[17,19,21] They also had healthier lifestyle habits as shown by low BMI and non-smoking habits; also noteworthy is the higher educational attainment found among patients seeking mixed and homeopathic GPs, which has been also previously reported in some[17,19] but not all related studies.[20,21] More educated people may be more knowledgeable about the side effects of

conventional psychotropic drugs and hence more likely to seek alternative treatments as suggested by Mac Lennan et al.[18]

With regard to the medical conditions, the EPI3 survey is one the few studies highlighting that sleep, anxiety and depressive disorders show similar burdens in terms of severity and impact on mental impairment regardless of practice modalities of GPs. As for prevalence, anxiety was confirmed as the most frequent mental health disorder encountered by alternative medicine practitioners, as previously reported.[5,10] Higher prevalence of patients suffering from depression seeking GP-CM might be attributed to the older age structure observed in this group when compared to those consulting GP-Ho: age trajectories observed for depression are often the opposite as those found for anxiety.[23] In spite of the fact that patients with depressive disorders in our study were less likely to seek strictly homeopaths than GP-CM, we must remember that depression is also one of the most commonly treated complaints as previously described for outpatient clinics of homeopathic hospitals in the UK National Health Service.[24]

Studies examining representative samples of general population seeking care for SADD have consistently shown that a large proportion of subjects are not treated with psychotropic drugs.[25,26] Conversely, psychotropic drugs use is frequently reported by subjects without identified psychiatric disorders.[27] This latter observation is probably the reason why there is an increasing trend for patients falling into the mixed category with similar characteristics and SADD. It is as if they sought a combination of both homeopathy and conventional medicines to fulfil individualised and holistic therapies needs and expectations, whilst being sure that good standards of medical and scientific practice were met.[28] This type of patients seems to be primarily concerned by associating their need for care and adequate treatment. One third of the patients with SADD consulting a GP-Mx received concomitantly homeopathic medicines and a psychotropic drug: this might suggest that homeopathic medicines could be prescribed not only as a substitute of unnecessary conventional psychotropic drugs, but also viewed as an adjunct to efficient psychotropic drugs;[10,20,29] such combination has been found to potentially help patients to accept and

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improve their symptoms[30] whilst avoiding some possible side effects of additional conventional therapies. Although no conclusions can be drawn at this stage on the outcome of consultations to GP-Mx and GP-Ho and whether their patients were given adequate treatment, our study highlights a genuine will from GP-Mx and GP-Ho to tailor therapies to their patients while avoiding unnecessary prescriptions.

High CAMBI scores, representing greater trust and belief in CAM, were found in the GP-Ho group, particularly in the subscales related to belief in natural treatments and holistic medicine and to a lesser degree in the patient's participation subscale. Patients of the GP-Mx group exhibited only a modest preference for natural treatments and holistic medicine with no difference overall towards patients seen by physicians practicing strictly conventional medicine. The different findings might be explained by the fact that GP-Ho operate a labelled practice in France (they must be certified homeopaths) which is not the case for the GP-Mx group defined specifically for this study. Our results provide interesting evidence of criterion validity for the CAMBI scale outside the United Kingdom. As for the quality of life scale (SF-12), patients scored similarly on the mental health subscale across all three groups of GPs, a result that was consistent with the similar number of comorbidities declared by treating physicians. Some studies found that patients seeking CAM therapies showed more QoL impairment than patients seeking conventional therapies.[31] Other studies, including ours, suggest that, despite the modality of practice (CAM or conventional therapies), GPs treat patients exhibiting similar mental health problems and disease burden.[32] Around 75% of patients who sought GPs exhibited additional morbidities in the EPI3 survey. The role of comorbidity in producing further burden from sleep, anxiety and depressive disorders has not been studied in patients attending GPs practising different modalities of treatment.[33,34] Integrating research to understand the role of comorbidity in QoL is challenging due to differences across studies in QoL conceptualisation, validity of QoL measurement, recruitment context (e.g., epidemiological, treatment-seeking), and consideration of socio-demographic and clinical predictors. Studies generally account for a limited range of comorbidity attributes, typically the presence versus

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3 absence of comorbidity, which loses the richness of information inherent in psychiatric
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5 presentations.
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8 Together with a lower number of visits to GPs and a lower proportion of prescribed psychotropic
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10 drugs in the GP-Ho group, our findings may have relevant public health implications. For instance,
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12 the National Institute for Health and Clinical Excellence (NICE), highlighted recently that the severity
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14 of depression at which antidepressants show consistent benefits over placebo is poorly defined,
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16 emphasising that, in general, the more severe the symptoms, the greater the benefit.[35] A patient-
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18 level meta-analysis demonstrated a lack of efficacy for antidepressants in the majority of patients
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20 with anxiety and depressive disorders.[3,4] Thus, the real impact of conventional antidepressants in
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22 this population is considerable, with adverse reactions outweighing potential benefits.[36] The
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24 patient's dissatisfaction with psychotropic drugs is one of the reasons cited for seeking other
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26 treatment options[37] and patients with a history of depression are more likely to seek CAM than
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28 those who have never been depressed before.[38]
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30 Under a primary care system designed for acute rather than chronic care, where clinicians "routinely
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32 experience the tyranny of the urgent",[39] our results suggested that management of SADD by GP-
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34 Ho was associated with less visits to the GP in the previous year but no more consultations to
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36 specialists than GP-CM. Medico-economic studies are needed to assess the patterns of access to and
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38 management by these different practitioners, which would contribute to better plan resource
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40 allocation for mental health services and target key groups for interventions in prevention, as far as
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42 severity of SADD is concerned.
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47 48 **Strengths and limitations of the study** 49

50 The present study examined a relatively large number of primary care practices in order to provide a
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52 real-world picture of CAM and homeopathic practice within the French primary care setting. The
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54 main strengths of the EPI3 survey have already been acknowledged elsewhere.[2] These include high
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56 representativeness of the patients involved and comparability against other nationwide studies. The
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weighted geographical distribution of the participating GPs in the survey was similar to the national distribution of GPs in private practice across the 22 French regions surveyed, and the distribution of physicians' individual characteristics regarding age, gender, type of contract with national health insurance and modality of practice differed only slightly from national statistics.[40]

The main limitation of our study relates to its cross-sectional design which does not allow addressing the directionality of the associations described between characteristics of patients and the type of medical practice of their physician. For instance, the healthier lifestyle observed among patients of the GP-Ho group could result from a selection bias (more educated patients tend to consult more GP-Ho) or from the homeopathic practice itself. Another limitation relates to the classification of GPs, which relied on self-reporting of CAM prescriptions. The definition of GP-Ho was more accurate and based on their professional certification. Therefore, generalisations of the results must be made cautiously, since our findings represented general practice in France. Nevertheless, this particular setting can be otherwise interpreted also as a strength, because it provided a unique opportunity to compare head-to-head primary care practices differing only by preferences for homeopathy and CAM, whereas all participant physicians shared similar medical professional status and basic training in conventional medicine. We feel that albeit the context of the study was specific to one country, differences between the groups of patients provided reliable information on the differential utilisation of homeopathy and CAM.

Finally, the fact that the participants were recruited in primary care might have excluded people with severe psychiatric disorders. This potential bias was likely to underestimate the prevalence of psychotropic drug use. However, prescriptions for psychotropic drugs were similar to those found in other French studies.[41,42]

CONCLUSION

The EPI3 survey is one of the largest studies to date conducted in general practice to describe attitudes and burden of sleep, anxiety and depressive disorders in patients seeking care from GPs with different prescribing preferences towards CAM and homeopathic practices. Our results showed

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3 that patients with SADD, while differing principally in their socio-demographic profiles and
4
5 conventional psychotropic prescriptions, were actually rather similar regarding the severity of SADD
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7 in terms of comorbidities and QOL. Further research is needed to explore potential benefits, both in
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9 terms of health economics and care, of consulting GPs that combine CAM and CM daily in the clinical
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11 management of SADD.
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14 **Competing interests**
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32 **Contributors**
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34
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37 DG, BA, GD, A-MM, MR and LA conceived both the research theme and the methods, analysed the
38
39 data and interpreted the results. LG-B implemented the trial in France, analysed the data, and
40
41 together with FL, PE and LA drafted and revised the paper. All members of the EPI3-LA-SER group
42
43 designed the study. A Fabre and PE analysed the data. All authors have contributed to, read and
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45 approved the final manuscript. LG-B is guarantor for the study. LG-B, PE and LA had full access to all
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47 of the data in the study and take responsibility for the integrity of the data and the accuracy of the
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49 data analysis.
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54 **Data sharing statement**
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56 No additional data available.
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Who seeks primary care for sleep, anxiety and depressive disorders from physicians prescribing homeopathic and other complementary medicine? Results from the EPI3 population survey.

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Abstract

Objectives: To describe and compare patients seeking treatment for sleep, anxiety and depressive disorders (SADD) from physicians in general practice (GPs) with three different practice preferences: strictly conventional medicine (GP-CM), mixed complementary and conventional medicine (GP-Mx), and certified homeopathic physicians (GP-Ho).

Design and setting: The EPI3 survey was a nationwide, observational study of a representative sample of general practitioners and their patients, conducted in France between March 2007 and July 2008.

Participants: 1572 patients diagnosed with SADD.

Primary and secondary outcomes: Patients' attitude towards complementary and alternative medicine (CAM); psychotropic drug utilisation.

Results: Compared to patients attending GP-CM, GP-Ho patients had healthier lifestyles whilst GP-Mx patients showed similar profiles. Psychotropic drugs were more likely to be prescribed by GP-CM (64%) than GP-Mx (55.4%) and GP-Ho (31.2%). The three groups of patients shared similar SADD severity.

Conclusion: Our results showed that patients with SADD, whilst differing principally in their socio-demographic profiles and conventional psychotropic prescriptions, were actually rather similar regarding the severity of SADD in terms of comorbidities and QOL. This information may help to better plan resource allocation and management of these common health problems in primary care.

Article summary

Article focus

- Up to 20% of patients attending primary healthcare in developed countries suffer from the often linked anxiety and depression disorders.

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- Conventional treatments, particularly antidepressants and anxiolytics, are widely prescribed; often associated with adverse side effects, conventional treatments are a likely cause for an increasing number of patients to choose homeopathy and other complementary therapies.
- Understanding the characteristics of physicians and patients, prescribing or using homeopathy, respectively, in conjunction with or instead of psychotropic drugs is undoubtedly of clinical and public health relevance.

Key messages

- Our results suggest that patients experiencing SADD who chose a GP with a clear orientation towards homeopathy, differed in their socio-demographic profile but not in the severity of their mental illness from those attending regular GPs with prescribing preferences towards conventional psychotropic drugs.
- Our survey is one the few studies highlighting that sleep, anxiety and depressive disorders show similar burdens in terms of severity and impact on mental impairment regardless of GPs' prescribing preferences.
- Our results showed that patients with SADD, whilst differing principally in their socio-demographic profiles and conventional psychotropic prescriptions, were actually rather similar regarding the severity of SADD in terms of comorbidities and QOL

Strengths and limitations

- Strengths of the EPI-3 study include high representativeness of the patients involved and comparability against other nationwide studies.
- The main limitation of our study relates to the classification of GPs, which relied on self-reporting of complementary and alternative medicine (CAM) prescriptions; generalisations of the results must be therefore made cautiously since our findings relate to general practice in France.

INTRODUCTION

Mental health problems such as sleep, anxiety or depressive disorders (SADD) are responsible for considerable disability worldwide[1] resulting in serious quality of life impairment[2] and are often associated with high use of medical services. It is estimated that up to 20 percent of patients attending primary healthcare in developed countries suffer from the often linked disorders of anxiety and depression. A high prescription rate of conventional therapies, particularly antidepressants,[3,4] which are often associated with adverse side effects, are a likely cause for an increasing number of patients to choose homeopathy and other complementary therapies.[5]

Evidence of effectiveness of these therapies compared to conventional psychotropic drugs is still limited.[6-8] Nonetheless, their perceived safety may be an important factor motivating patients with SADD disorders to seek care from GPs preferring homeopathy and other types of complementary medicine. Among complementary alternative medicine (CAM) modalities of practice, homeopathy is widely used in countries with large access to conventional medicine and represents a particularly good marker for CAM practice in France, where homeopathic drugs are partly reimbursed by national health insurance and prescribed only by a medical practitioner, if not purchased as over-the-counter drugs.[9] In a previous study,[10] homeopathic practitioners (including non-medical healthcare professionals) indicated that their patients used homeopathy mainly in association with conventional psychotropic treatments, psychotherapy and counselling in a mixed practice.

Understanding the characteristics of physicians and patients, prescribing or using homeopathy, respectively, in conjunction with or instead of psychotropic drugs is undoubtedly of clinical and public health relevance. The objective of this study was to describe and compare patients seeking treatment for sleep, anxiety and depressive disorders (SADD) from physicians in general practice

(GPs) with three different practice preferences: strictly conventional medicine (GP-CM), mixed complementary and conventional medicine (GP-Mx), and certified homeopathic physicians (GP-Ho).

METHODS

Study design, settings and participants

The EPI3 survey was a nationwide, observational study of a representative sample of general practitioners and their patients, conducted in France between March 2007 and July 2008. The methodology of the study has been described elsewhere.[2]

Participants (GPs and their patients) were drawn by applying a two-stage sampling process. The GPs were first randomly selected from the French national directory of physicians and invited to participate, which meant allowing a research assistant to conduct a one-day survey in the waiting room at the doctor’s practice. Blind to the study focus on conventional and complementary alternative medicine (CAM) practice, consenting GPs were next contacted by telephone to enquire how frequently they prescribed CAM (homeopathy, mesotherapy, acupuncture, phytotherapy, etc.). Depending on their prescribing preferences towards homeopathic medicines, they were classified as: strictly conventional GPs (GP-CM), who declared themselves never or rarely using CAM or homeopathic medicines; mixed practice (GP-Mx), who were GPs declaring using CAM regularly; and GPs certified in homeopathic practice (GP-Ho). In France, homeopathy can only be prescribed by physicians, mostly GPs qualified as homeopaths by the French National Council of Physicians (CNOM) upon completion of specific training and certification (3.3% of all French GPs in 2008).[11]

The second stage of selection consisted of random one-day sampling of consultations per participating physician, in order to survey all patients attending the practice on that very day. All adults (18 years old and over) and accompanied minor patients were eligible for inclusion in the EPI3 survey, except those whose health status or literacy level did not allow responding to a self-administered questionnaire.

During the consultation, GPs asked all adult patients diagnosed or suspected of suffering SADD whether they would volunteer for a more in-depth study of their disease. Consenting patients were contacted again within 72 hours for a telephone interview conducted by trained interviewers.

Data collection

Collection of data from patients included: age, gender, nationality, educational attainment, type of health insurance, additional private insurance, smoking habit, alcohol intake, physical activity, height, weight, employment status, familial status, previous number of visits and referrals to physicians.

Participants were also asked to confirm whether the attending GP was their regular primary care physician or not. In France, all citizens are required to choose a GP as their regular physician. This study was based on patients who reported being seen exclusively by their regular family physician.

Health-related quality of life was assessed using the validated 12-item Short Form (SF-12) questionnaire,[12] allowing estimation of physical health (PCS score) and mental health (MCS score); the SF-12 questionnaire was validated in the late 90s for use in the US, the UK, France and many other European countries.[13] Patients also completed the Complementary and Alternative Medicine Beliefs Inventory (CAMBI), which assesses attitudes and expectations of patients towards medical care, participation in decision making, perception of risks associated with treatment, and understanding of both illness and healing process via a 17-question inventory.[14] High scores on the CAMBI items indicate pro-CAM treatment belief.

GPs recorded the main reason for consultation and up to five other diagnoses present that day as well as their prescriptions, which were entered by the interviewer in a database that automatically recorded the corresponding ATC (Anatomical Therapeutic Chemical) codes, revision 2009. Diagnoses relating to 100 diseases[2] were coded by a trained archivist using the 9th revision of the International Classification of Diseases.[15] Patients with the following ICD codes were classified as anxious: 300.0 anxiety states; 300.2 phobic disorders; 300.3 obsessive-compulsive disorders; 300.5 neurasthenia; 300.8 somatoform disorders; 306.2 psychogenic disease related to underlying physiological disorders. Patients with the following ICD codes were classified as depressive: 296.3

major depressive disorder, recurrent episode; 296.5 bipolar disorder, most recent episode depressed; 296.1 manic disorder; 296.6 manic-depressive psychosis; 300.4 dysthymic disorders; 300.5: neurasthenia; 309.0 adjustment reaction, 309.1 prolonged depressive reaction, 311.9 unclassified depressive disorders. Patients were considered as experiencing sleep disorders if their diagnoses related to ICD codes 307.4 (specific disorders of sleep of non-organic origin) and 780.5 (sleep disturbances).

Comorbidity was defined as the presence of at least one diagnosis other than the principal motive for consultation at the recruitment visit. Comorbidities were categorised as: co-associated sleep, anxiety, or depressive disorder (other than the main reason for consultation), musculoskeletal disorders, respiratory diseases, cardiovascular and metabolism disorders, diabetes, thyroid and endocrine disorders, and finally digestive disorders. Severity of SADD was characterised firstly by degree of quality of life (QoL) impairment, then by the presence and finally by number of associated comorbidities.

Statistical analysis

Characteristics of non-participants (age, gender, length of time attending the GP’s medical practice, type of health insurance and main reasons for consultation) were used to calibrate the final sample as previously reported[2] to ensure that it would closely represent the whole population attending French GPs practices, using a method known in demographic studies as the CALMAR procedure.[16] Overall characteristics of patients seeking access to each of the three types of GP and results reported here were based on weighted data. Distributions were compared using Chi-Square and Fisher tests for categorical variables and Student and Wilcoxon tests for continuous variables.

Multiple logistic regression analyses were used to compare patients in the GP-CM group to GP-Mx and GP-Ho groups for categorical variables and were adjusted for all variables listed in Table 1 to control for potential confounding.

The GP-Mx and GP-Ho groups were compared to the GP-CM group for patients' exposure to antidepressants (ATC codes beginning with N06AB, N06AX, N06AA and N06AF), anxiolytics and hypnotics (ATC codes beginning with N05BA, N05BB, N05BX, N05BE, N05CD, N05CF and N03AE) mood normalisers (N05AN, N03AG) and antipsychotics (ATC codes beginning with N05AK, N05AA, N05AB, N05AC, N05AD, N05AF, N05AG, N05AH, N05AL, N05AX, N07XX) as well as homeopathic preparations specifically prescribed for SADD symptoms.

ANCOVA analyses were performed to provide mean scores for the SF-12 mental (MCS) and physical scales (PCS) adjusted for age (<40, 40-60, 60+ years), gender, marital status, employment status, body mass index (BMI), number of associated comorbidities (other than SADD), and finally associated SADD (other than the main diagnose, yes/no). MCS score and PCS score were categorised into quartiles corresponding to: 34.1 (Q1), 42.4 (Q2), and 48 (Q3) for MCS; 39.3 (Q1), 47.3 (Q2) and 54.2 (Q3) for PCS.

Associations between scores from each of the 17 questions of the CAMBI questionnaire and the probability of attending a GP-Mx or GP-Ho as compared to a GP-CM were computed after adjusting for age, gender and educational level. Scores obtained per question, ranging from 1 (totally disagree) to 7 (totally agree), were dichotomised in order to further distinguish participants clearly in favour (scoring 5 to 7) or in disagreement (scoring 1 to 3) with the 17 CAMBI questions. Each of the three subscales scores and the total CAMBI score were then dichotomised according to the 75th percentile (40, 26 and 33, respectively; 96 for the total score).

The possibility of a clustering effect at the practice level was tested using Generalised Estimating Equations (GEE) multivariate models. All the analyses were performed with SAS software version 9.1 (SAS Institute, Inc., Cary, North Carolina).

The study was approved by the French National Data-Protection Commission (CNIL) and the CNOM. Participating physicians received compensation fees for recruiting patients but not patients.

RESULTS

A total of 825 GPs participated in the survey. There was no difference between the three groups of GPs for age (mean = 50.7 years) but GP-Ho and GP-Mx were more often women than GP-CM (48.9% and 31.5% versus 20.3%, respectively), and less often salaried (14.3% and 16.9% versus 34.5%, respectively). In addition, GP-Ho were more likely to practise alone than GP-CM and GP-Mx (72.4% versus 51.8% and 55.9%, respectively) (all differences statistically significant). Among the 11 701 patients attending the doctor’s office on the survey day, 8652 (73.9%) agreed to participate and complete information was collected for 8559 (73.1%) patients. Compared to non-participants, participants were more often women (62.7% and 56.8%, respectively), younger (mean age 43.3 and 47.7, respectively) and more likely to consult for a SADD (20.6% and 11.6%, respectively). Of the 6379 who declared the consulting physician as their regular GP, 1572 met the inclusion criteria and were included in the analyses with the following diagnoses: anxiety (n=370), depression (n=583), sleep disorders (n=480) or SADD of undetermined cause (n=139).

Compared to the GP-CM group, patients from the GP-Mx group showed similar characteristics but those from the GP-Ho group were more frequently younger, more educated, employed women living with children or a spouse (Table 1). They also had a healthier lifestyle with lower BMI, and were more frequently non-smokers and occasional or non-consumers of alcohol. They declared however less visits to their regular GP in the previous year. Motives of consultation showed more anxiety and less depression in the GP-Ho group than in the two others but the distribution was unremarkable otherwise. Physicians prescribing preferences were confirmed with the GP-Ho group using more homeopathy and less psychotropic drugs than the two other groups. The GP-Mx group however did not differ much from the GP-CM group.

Table 1. Characteristics of patients seeking care for SADD according to the type of practice of their regular GP (EPI3 Survey, n=1572)

	GP-CM (n=410) N, weighted %	GP-Mx (n=718) N, weighted %	GP-Ho (n=444) N, weighted %
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Gender						
Females vs. Males	269	64.7	500	68.9	323	72.6*
Age categories (years)						
18-39	92	20.7	195	26.7	131	28.8*
40-59	163	38.9	298	41.3	193	43.6*
60 and over	155	40.4	225	32.0	120	27.6*
Employment status						
Employed	171	39.5	353	48.9	240	53.5*
Educational level						
Secondary school not completed	93	22.1	177	22.9	158	35.2*
Universal Health Insurance coverage (CMU)						
	36	9.5	65	9.8	26	6.5
Familial status						
Living with children	164	38.1	306	42.5	195	44.1*
Living with a spouse	239	56.6	439	61.2	285	64.0*
Body Mass Index (%)						
<25	216	52.1	413	57.9	302	67.9*
25-30	124	30.9	186	25.6	106	24.0*
>30	70	17.0	119	16.6	36	8.1*
Tobacco consumption (%)						
Never smoked	195	48.4	365	50.8	251	57.1*
Past smoker	111	26.9	170	23.6	112	24.6*
Current smoker	104	24.8	183	25.6	81	18.3*
Alcohol Consumption (%)						
Never	152	37.4	287	40.0	142	32.4
Sometimes	193	46.4	354	49.3	254	56.2
Daily	65	16.3	77	10.7	48	11.4
Physical exercise (%)						
> 30 minutes / day	125	30.7	207	29.3	140	31.6
Number of visits to regular GP during the last year						
None	7	1.7	16	2.3	10	2.2
1-6	228	55.4	405	57.0	296	66.8*
7-12	142	34.6	234	32.1	114	25.6*
12 and over	33	8.4	63	8.7	24	5.4*
Number of visits to a specialist during the last year						
None	105	25.8	200	28.0	113	25.6
1	114	27.0	206	28.6	137	31.2
2	63	15.6	133	18.4	82	18.1
2+	128	31.5	179	25.0	112	25.1
Motive for consultation (ICD-9)						
Anxiety	79	18.8	158	21.2	133	30.2*
Depression	171	41.1	284	39.6	127	28.7*
Sleep disorders	131	32.7	198	28.9	151	34.0
Unspecified	52	12.6	95	12.5	65	14.1
Treatment						
Any psychotropic drugs	266	64.0	404	55.4	138	31.2*
<i>Antidepressants</i>	152	36.0	231	31.5	73	16.5*
<i>Anxiolytics/hypnotics</i>	185	44.8	286	39.3	87	19.8*
<i>Antipsychotics</i>	11	3.1	25	3.5	10	2.4
<i>Normothymics</i>	16	3.9	7	1.1	20	4.6
Other conventional drugs	144	36.0	289	41.2	189	42.7
Homeopathic medicines for SADD	1	0.2	36	4.9	139	30.9*
Other homeopathic medicines	6	1.4	58	7.8	288	67.7*

Abbreviations: GP-CM: general practitioner strictly practising conventional medicine; GP-Mx: general practitioner with mixed practice; GP-Ho: general practitioner with a certification in homeopathic care.

*Difference with conventional medicine category statistically significant ($p \leq 0.05$) in logistic regression including all variables.

Considering the severity of mental health problem, the GP-Mx group had systematically less often an associated SADD comorbidity than in the two other groups but the distribution of comorbidities other than SADD was unremarkable otherwise between groups (Table 2). For quality of life, the mental score summary (MCS) of the SF-12 was similar across the three groups with no clinically or statistically meaningful difference (Table 3). The GP-Ho group however had a slightly better physical summary score (PCS) than the two other groups.

Table 2. Burden of associated comorbidity and other psychological distress in patients with sleep, anxiety, or depressive disorders according to the type of practice of regular GPs (EPI3 Survey, n=1572)

Comorbidities present at the medical visit	GP-CM Weighted%	GP-Mx Weighted%	Gp-Ho Weighted%
Patients with SADD (n=1572)*	n=410	n=718	n=444
Associated SADD comorbidity (other than primary)	7.4	2.6 ⁺	5.3
At least one other comorbidity	74.3	68.7	69.5
MSD	27.1	23.8	24.8
Respiratory diseases	16.6	11.7	18.5
Cardiovascular and metabolism disorders	35.1	30.2	22.9 ⁺
Diabetes, thyroid and endocrine disorders	12.7	9.6	8.1
Digestive disorders	11.9	11.5	11.5
Patients with depression (n=583)	n=171	n=285	n=127
Associated SADD comorbidity (other than depression)	13.7	3.7 ⁺	10.0
At least one other comorbidity	75.2	67.3 ⁺	70.6 ⁺
MSD	29.2	23.2	28.6
Respiratory diseases	15.3	9.8 ⁺	12.8
Cardiovascular and metabolism disorders	36.5	30.4	21.6 ⁺
Diabetes, thyroid and endocrine disorders	13.0	10.8	7.9 ⁺
Digestive disorders	10.4	9.0	10.6
Patients with anxiety (n=370)	n=79	n=158	n=133
Associated SADD comorbidity (other than anxiety)	12.9	5.7 ⁺	13.6
At least one other comorbidity	71.2	72.2	62.2 ⁺
MSD	22.5	26.5	25.2
Respiratory diseases	14.3	9.8	14.2
Cardiovascular and metabolism disorders	23.6	31.2 ⁺	22.3

<i>Diabetes, thyroid and endocrine disorders</i>	10.7	11.7	9.3
<i>Digestive disorders</i>	18.1	15.0	13.7

Patients with sleep disorder (n=480)	n=131	n=198	n=151
Associated SADD comorbidity (other than sleep disorder)	9.8	3.7	9.7
At least one other comorbidity	71.3	63.6	67.6
<i>MSD</i>	29.7	22.0	21.9 ⁺
<i>Respiratory diseases</i>	14.3	12.7	21.2
<i>CV and metabolism disorders</i>	37.8	28.9	19.4
<i>Diabetes, thyroid and endocrine disorders</i>	10.4	5.6 ⁺	4.4 ⁺
<i>Digestive disorders</i>	10.2	10.7	12.1

Abbreviations: GP-CM: general practitioner strictly practising conventional medicine; GP-Mx: general practitioner with mixed practice; GP-Ho: general practitioner with a certification in homeopathic care; MSD: musculoskeletal disorders; SADD: sleep, anxiety or depressive disorders.

*Including missing diagnosis (according to ICD9) values (n=139 patients).

+Difference with conventional medicine category statistically significant ($p \leq 0.05$) in logistic regression including age (<40, 40-60, 60+ years), gender, marital status, employment status, BMI (body mass index: <25; 25-30; >30kg/m²), MCS: SF12-Mental Component Summary score; PCS: SF12-Physical Component Summary score.

Table 3. Adjusted quality of life (MCS and PCS) of patients visiting their regular GP according to the type of practice (EPI3 Survey, n=1572)

Quality of Life SF-12	GP-CM Mean (sd)*	GP-Mx Mean (sd)*	p-value*	GP-Ho Mean (sd)*	p-value*
SADD					
MCS	35.3 (1.0)	35.9 (1.0)	0.64	36.4 (1.0)	0.24
PCS	42.3 (1.0)	42.9 (1.0)	0.58	45.4 (1.0)	<0.001
Anxiety					
MCS	36.7 (1.4)	35.8 (1.2)	0.73	37.3 (1.2)	0.88
PCS	44.1 (1.4)	44.8 (1.2)	0.81	47.4 (1.3)	0.03
Depression					
MCS	34.5 (1.4)	34.6 (1.5)	0.99	34.0 (1.6)	0.92
PCS	40.5 (1.5)	41.9 (1.5)	0.29	44.1 (1.6)	0.006
Sleep disorders					
MCS	34.6 (1.6)	37.0 (1.6)	0.06	35.7 (1.7)	0.64
PCS	44.4 (1.6)	44.3 (1.7)	0.99	47.5 (1.7)	0.03

Abbreviations: GP-CM: general practitioner strictly practising conventional medicine; GP-Mx: general practitioner with mixed practice; GP-Ho: general practitioner with a certification in homeopathic care; MSD: musculoskeletal disorders; MCS: SF12-mental component summary score; PCS: SF12-physical component summary score SADD: sleep, anxiety or depressive disorders.

*from ANCOVA adjusted for age (<40, 40-60, 60+ years), gender, marital status, employment status, BMI, number of associated comorbidities (other than main SADD), SADD comorbidity (yes/no); a higher score indicates better health.

The attitudes towards complementary medicine estimated by CAMBI (Table 4) showed that patients in the GP-Ho group had a probability of scoring high (favourable to CAM) over three times that of the GP-CM group (Odds ratio (OR) = 3.65, 95% confidence interval (CI): 2.94-3.77). The result was consistent for each of the three CAMBI subscales with OR= 2.08 (95% CI: 1.78-2.32) for belief in natural treatment, OR= 1.43 (95% CI: 1.23-1.77) for active patient’s participation in care, and OR= 2.75 (95% CI: 2.55-3.24) belief in holistic medicine. CAMBI scores from patients of the GP-Mx group were comparable to the GP-CM group, although a slightly higher trust in natural treatment subscale was observed (OR = 1.15, 95% CI: 1.03-1.26).

Table 4. Attitudes of patients with SADD towards complementary medicine as measured by the CAMBI (attitudes towards complementary and alternative medicine beliefs inventory) questionnaire (EPI3 Survey, n=1572)

	Type of practice	
	GP-Mx vs. GP-CM OR* (95% CI)	GP-Ho vs. GP-CM OR* (95% CI)
1. Treatments should have no negative side effects	1.11 (0.94-1.33)	1.70 (1.43-1.93)
2. It is important to me that treatments are not toxic	0.85 (0.65-1.14)	1.55 (1.41-2.03)
3. Treatments should only use natural ingredients	1.07 (0.97-1.08)	2.02 (1.87-2.47)
4. It is important that treatments boost my immune system	1.12 (0.93-1.18)	1.65 (1.38-2.11)
5. Treatments should allow my body to heal itself	1.28 (1.13-1.38)	2.02 (1.77-2.18)
6. Treatments should increase my natural ability to keep healthy	1.05 (1.01-1.34)	1.54 (1.64-2.27)
7. Treatment providers should treat patients as equals	1.01 (0.89-1.17)	1.24 (1.08-1.67)
8. Patients should take an active role in their treatment	0.88 (0.81-1.06)	1.75 (1.18-1.81)
9. Treatment providers should make all decisions about treatment	0.85 (0.74-1.07)	1.37 (1.21-1.54)
10. Treatment providers should help patients make their own decisions about treatment	0.94 (0.86-1.11)	2.43 (1.89-2.43)
11. Treatment providers control what is discussed during consultations	1.04 (0.85-1.19)	1.37 (1.18-1.45)
12. Health is about harmonising your body, mind and spirit	1.08 (0.95-1.20)	2.33 (1.55-2.45)
13. Imbalances in people’s lives are a major cause of illness	1.15 (1.02-1.27)	2.07 (1.66-2.07)

14. Treatments should focus only on symptoms rather than the whole person	0.82 (0.78-1.04)	2.44 (1.75-2.45)
15. Treatments should focus on people's overall well-being	1.21 (1.01-1.44)	1.53 (1.48-1.95)
16. I think my body has a natural ability to heal itself	1.13 (0.95-1.22)	2.43 (1.70-2.22)
17. There is no need for treatments to be associated to natural healing power	1.00 (0.77-1.07)	1.56 (1.33-1.81)
CAMBI Total score >Q3	1.05 (0.92-1.29)	3.65 (2.94-3.77)
CAMBI sub-scores:		
• Natural treatment >Q3	1.15 (1.03-1.26)	2.08 (1.78-2.32)
• Patient's participation >Q3	0.95 (0.81-1.03)	1.43 (1.23-1.77)
• Holistic medicine >Q3	1.15 (0.95-1.17)	2.75 (2.55-3.24)

Abbreviations: GP-CM: general practitioner strictly practising conventional medicine; GP-Mx: general practitioner with mixed practice; GP-Ho: general practitioner with a certification in homeopathic care; OR: Odds ratio

*adjusted for age, gender and educational level.

DISCUSSION

To our knowledge, the EPI3 study is the first nationwide survey conducted in a large representative sample of patients to provide characteristics and attitudes, as well as the first to quantify quality of life and the burden of sleep, anxiety or depressive disorders (SADD) in patients seeking care from their regular GPs with different preferences towards CAM and homeopathic practices.

Our results suggest that patients experiencing SADD, and who chose a GP with a clear orientation towards homeopathy, differed in their socio-demographic profile but not in the severity of their mental illness from those attending regular GPs with prescribing preferences towards conventional psychotropic drugs. Patients with SADD attending a GP-Ho in our study were more likely to be female, as previously reported[17-20] except for one survey,[21] and younger; age as also been suggested by other authors,[22] although no such association has been described elsewhere.[17,19,21] They also had healthier lifestyle habits as shown by low BMI and non-smoking habits; also noteworthy is the higher educational attainment found among patients seeking mixed and homeopathic GPs, which has been also previously reported in some[17,19] but not all related studies.[20,21] More educated people may be more knowledgeable about the side effects of

conventional psychotropic drugs and hence more likely to seek alternative treatments as suggested by Mac Lennan et al.[18]

With regard to the medical conditions, the EPI3 survey is one the few studies highlighting that sleep, anxiety and depressive disorders show similar burdens in terms of severity and impact on mental impairment regardless of practice modalities of GPs. As for prevalence, anxiety was confirmed as the most frequent mental health disorder encountered by alternative medicine practitioners, as previously reported.[5,10] Higher prevalence of patients suffering from depression seeking GP-CM might be attributed to the older age structure observed in this group when compared to those consulting GP-Ho: age trajectories observed for depression are often the opposite as those found for anxiety.[23] In spite of the fact that patients with depressive disorders in our study were less likely to seek strictly homeopaths than GP-CM, we must remember that depression is also one of the most commonly treated complaints as previously described for outpatient clinics of homeopathic hospitals in the UK National Health Service.[24]

Studies examining representative samples of general population seeking care for SADD have consistently shown that a large proportion of subjects are not treated with psychotropic drugs.[25,26] Conversely, psychotropic drugs use is frequently reported by subjects without identified psychiatric disorders.[27] This latter observation is probably the reason why there is an increasing trend for patients falling into the mixed category with similar characteristics and SADD. It is as if they sought a combination of both homeopathy and conventional medicines to fulfil individualised and holistic therapies needs and expectations, whilst being sure that good standards of medical and scientific practice were met.[28] This type of patients seems to be primarily concerned by associating their need for care and adequate treatment. One third of the patients with SADD consulting a GP-Mx received concomitantly homeopathic medicines and a psychotropic drug: this might suggest that homeopathic medicines could be prescribed not only as a substitute of unnecessary conventional psychotropic drugs, but also viewed as an adjunct to efficient psychotropic drugs;[10,20,29] such combination has been found to potentially help patients to accept and

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2
3 improve their symptoms[30] whilst avoiding some possible side effects of additional conventional
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5 therapies. Although no conclusions can be drawn at this stage on the outcome of consultations to
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7 GP-Mx and GP-Ho and whether their patients were given adequate treatment, our study highlights a
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9 genuine will from GP-Mx and GP-Ho to tailor therapies to their patients while avoiding unnecessary
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11 prescriptions.

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13 High CAMBI scores, representing greater trust and belief in CAM, were found in the GP-Ho group,
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15 particularly in the subscales related to belief in natural treatments and holistic medicine and to a
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17 lesser degree in the patient's participation subscale. Patients of the GP-Mx group exhibited only a
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19 modest preference for natural treatments and holistic medicine with no difference overall towards
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21 patients seen by physicians practicing strictly conventional medicine. The different findings might be
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23 explained by the fact that GP-Ho operate a labelled practice in France (they must be certified
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25 homeopaths) which is not the case for the GP-Mx group defined specifically for this study. Our
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27 results provide interesting evidence of criterion validity for the CAMBI scale outside the United
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29 Kingdom. As for the quality of life scale (SF-12), patients scored similarly on the mental health
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31 subscale across all three groups of GPs, a result that was consistent with the similar number of
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33 comorbidities declared by treating physicians. Some studies found that patients seeking CAM
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35 therapies showed more QoL impairment than patients seeking conventional therapies.[31] Other
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37 studies, including ours, suggest that, despite the modality of practice (CAM or conventional
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39 therapies), GPs treat patients exhibiting similar mental health problems and disease burden.[32]
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41 Around 75% of patients who sought GPs exhibited additional morbidities in the EPI3 survey. The role
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43 of comorbidity in producing further burden from sleep, anxiety and depressive disorders has not
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45 been studied in patients attending GPs practising different modalities of treatment.[33,34]
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47 Integrating research to understand the role of comorbidity in QoL is challenging due to differences
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49 across studies in QoL conceptualisation, validity of QoL measurement, recruitment context (e.g.,
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51 epidemiological, treatment-seeking), and consideration of socio-demographic and clinical predictors.
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53 Studies generally account for a limited range of comorbidity attributes, typically the presence versus
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absence of comorbidity, which loses the richness of information inherent in psychiatric presentations.

Together with a lower number of visits to GPs and a lower proportion of prescribed psychotropic drugs in the GP-Ho group, our findings may have relevant public health implications. For instance, the National Institute for Health and Clinical Excellence (NICE), highlighted recently that the severity of depression at which antidepressants show consistent benefits over placebo is poorly defined, emphasising that, in general, the more severe the symptoms, the greater the benefit.[35] A patient-level meta-analysis demonstrated a lack of efficacy for antidepressants in the majority of patients with anxiety and depressive disorders.[3,4] Thus, the real impact of conventional antidepressants in this population is considerable, with adverse reactions outweighing potential benefits.[36] The patient's dissatisfaction with psychotropic drugs is one of the reasons cited for seeking other treatment options[37] and patients with a history of depression are more likely to seek CAM than those who have never been depressed before.[38]

Under a primary care system designed for acute rather than chronic care, where clinicians "routinely experience the tyranny of the urgent", [39] our results suggested that management of SADD by GP-Ho was associated with less visits to the GP in the previous year but no more consultations to specialists than GP-CM. Medico-economic studies are needed to assess the patterns of access to and management by these different practitioners, which would contribute to better plan resource allocation for mental health services and target key groups for interventions in prevention, as far as severity of SADD is concerned.

Strengths and limitations of the study

The present study examined a relatively large number of primary care practices in order to provide a real-world picture of CAM and homeopathic practice within the French primary care setting. The main strengths of the EPI3 survey have already been acknowledged elsewhere.[2] These include high representativeness of the patients involved and comparability against other nationwide studies. The

weighted geographical distribution of the participating GPs in the survey was similar to the national distribution of GPs in private practice across the 22 French regions surveyed, and the distribution of physicians' individual characteristics regarding age, gender, type of contract with national health insurance and modality of practice differed only slightly from national statistics.[40]

The main limitation of our study relates to its cross-sectional design which does not allow addressing the directionality of the associations described between characteristics of patients and the type of medical practice of their physician. For instance, the healthier lifestyle observed among patients of the GP-Ho group could result from a selection bias (more educated patients tend to consult more GP-Ho) or from the homeopathic practice itself. Another limitation relates to the classification of GPs, which relied on self-reporting of CAM prescriptions. The definition of GP-Ho was more accurate and based on their professional certification. Therefore, generalisations of the results must be made cautiously, since our findings represented general practice in France. Nevertheless, this particular setting can be otherwise interpreted also as a strength, because it provided a unique opportunity to compare head-to-head primary care practices differing only by preferences for homeopathy and CAM, whereas all participant physicians shared similar medical professional status and basic training in conventional medicine. We feel that albeit the context of the study was specific to one country, differences between the groups of patients provided reliable information on the differential utilisation of homeopathy and CAM.

Finally, the fact that the participants were recruited in primary care might have excluded people with severe psychiatric disorders. This potential bias was likely to underestimate the prevalence of psychotropic drug use. However, prescriptions for psychotropic drugs were similar to those found in other French studies.[41,42]

CONCLUSION

The EPI3 survey is one of the largest studies to date conducted in general practice to describe attitudes and burden of sleep, anxiety and depressive disorders in patients seeking care from GPs with different prescribing preferences towards CAM and homeopathic practices. Our results showed

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that patients with SADD, while differing principally in their socio-demographic profiles and conventional psychotropic prescriptions, were actually rather similar regarding the severity of SADD in terms of comorbidities and QOL. Further research is needed to explore potential benefits, both in terms of health economics and care, of consulting GPs that combine CAM and CM daily in the clinical management of SADD.

For peer review only

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Competing interests

LG-B, PE, BA, MR and LA's institution received support from Boiron for the submitted work; FR and DG received a consulting fee or honorarium from LA-SER for the submitted work; BB, FL, JM, GD and A-MM have no relationships with Boiron or any other companies that might have an interest in the submitted work in the previous 3 years; LG-B, PE, BA and MR are employees of LA-SER, the company conducting the study; LA is a stockholder in LA-SER; LG-B was the recipient of a research fellowship from INSERM (French National Institute of Health and Medical Research) at the time of the study.

Contributors

The work presented here was carried out with the involvement of every author. LG-B, BB, FL, FR, JM, DG, BA, GD, A-MM, MR and LA conceived both the research theme and the methods, analysed the data and interpreted the results. LG-B implemented the trial in France, analysed the data, and together with FL, PE and LA drafted and revised the paper. All members of the EPI3-LA-SER group designed the study. A Fabre and PE analysed the data. All authors have contributed to, read and approved the final manuscript. LG-B is guarantor for the study. LG-B, PE and LA had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Data sharing statement

No additional data available.

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Contributing members of the EPI3-LASER study group are:

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What drives patients with sleep, anxiety or depressive disorders to seek care from general practitioners with preference for homeopathy and other complementary medicines? Results from the EPI3 population survey.

All changes to the manuscript originally submitted have been underlined on the revised version manuscript being currently resubmitted for easier identification

Reviewer(s)' Comments to Author:	Author's replies
GENERAL COMMENTS, TITLE & ABSTRACT	
<p>REV. #1: The type of study should be specified to "cross sectional" and the word "association" used to make it clear that no causal inference can be drawn. E.g. the aim in the abstract uses "determinants" which indicate a prospective design.</p> <p>REV. #2: The main weakness is reflected in the title as the paper claims to answer the question of what "drives" patients to seek care. The term <i>determinants</i> assumes that the factors associated with CAM use are precursors rather than products of use. Perhaps if the focus was on uncovering the profiles of people with SAAD with regards to their care-seeking choices this problem could be avoided.</p>	<p>We fully agree and had no intention of performing a longitudinal analysis with this cross-sectional design. <u>Terms have been changed as suggested and the title rephrased accordingly.</u> However, we decided to keep the verb 'seek' in the title and the text as we believe that it does not imply any directionality within analyses or interpretation of results.</p>
<p>REV. #1: The aim in the abstract and text is different. I would suggest rephrasing to something similar to: "Investigating the characteristics, health status, treatment and attitudes towards CAM for patients with SADD visiting..."</p>	<p><u>The objective has been standardised and rephrased so as to better reflect the cross-sectional nature of the study.</u></p>
<p>REV. #1: The abbreviation EPI3 is not written in full any place. I personally think EPI3 should be omitted and replaced with "this study".</p>	<p>The EPI3 abbreviation (equivalent to the name of the general study) has no other specific meaning than referring to an epidemiological survey which focussed on three groups of common motives for consultation in primary care (SADD, musculoskeletal disorders and upper respiratory tract infections). We think it is important to maintain the name of the study for citation purposes (as it is often done in other large studies).</p> <p><u>No change suggested</u> – please advise otherwise.</p>
<p>REV. #1: Sometimes the term "GP-allo" is used</p>	<p><u>Terms and abbreviations have been standardised</u></p>

instead of "GP-CM"	<u>throughout the revised manuscript.</u>
METHODS	
REV. #1: Please include a sentence or two more about how the patients choose their GP, is there any previous data suggesting that patients select GPs based on the GPs prescribing preferences?	It was the objective of the study to better understand who consults who based on utilisation of CAMs and homeopathy, as there is no information in France on how patients select their GPs. Prescribing preferences were obtained from participating physicians at the time of their inclusion in the study therefore, except for GP-Ho who are certified homeopaths, patients did not necessarily know the differences between GP-CM and GP-Mx in terms of type of practice. <u>No change suggested</u> – please advise otherwise.
REV. #1: Page 10, line 47. Propensity should be probability (I thought first that it referred to propensity scores).	<u>Change made as proposed.</u>
RESULTS	
REV. #1: It is not evident throughout the article that the comparison is between GP-CM and the two other groups. As there are few differences between GP-CM and GP mixed, this could be presented in a separate section and the rest of the text could then focus on the GP-CM vs GP-Homeo comparison.	GP-CM group is the reference against which the other two groups are compared in all analyses. <u>Changes have been made in the abstract, statistical methods and results (entirely revised – see below) sections to help clarify that aspect.</u>
REV. #1: Much of the text in the result section is repetition of what is found in the tables, presented in a way that makes it difficult to find what the main findings are. I suggest to shorten the text by only presenting the main findings.	The text has been shortened with emphasis on main findings (<u>changes have not been underlined as the whole section was shortened</u>).
REV. #1: There is no presentation of the number of GP and their characteristics. This should be included in the start of the result section.	Information has been added to the first <u>paragraph of results</u> .
REV. #1: A flow chart of the patients would be helpful. I find the CONSORT guidelines for non-pharmacological trials to be relevant for showing both patient and providers.	Given this was a general survey, specific motives for non-participation were not collected. We feel that the participation rate of 73.1% was quite exceptional considering the type of health survey and that a flow chart would not contribute to further clarify potential biases (see also below). <u>No change suggested</u> - please advise otherwise.
REV. #1: Some information about non-respondents should be given in results and	Information added to the first paragraph of <u>results</u> .

mentioned in discussion.	
DISCUSSION	
<p>REV. #2: Some mention could be made of the need to disentangle whether CAM promotes healthier lifestyles or if it only appeals to people with healthier lifestyles, or both (which based on the literature and health behavior change theory) is the more likely option.</p> <p>The literature that is consistent with this finding should be presented and discussed: Is the healthy lifestyle a product or precursor of CAM use? Can the authors speculate on this point based on previous research in this area? The “drive” part of the research question cannot really be answered (See Sirois & Gick, 2002, Sirois & Purc-Stephenson, 2008, Nahin et al. 2007, Sharpe 2007 and Willams-Peiohata 2012 for more on this issue).</p>	<p>We fully agree. <u>The cross-sectional nature of this study (as in the majority of this domain) has been highlighted in the discussion (second paragraph of the discussion).</u></p> <p>We feel that the literature suggested is not directly applicable to our setting where all consultants were physicians with various degrees of preference for utilisation of homeopathy. The article cited refers mainly to types of CAM and preferences to health consultants rather than physicians.</p> <p><u>No change suggested.</u></p>
<p>REV. #2: Why is there no discussion of the results of the CAMBI analyses? Even if only one subscale showed sig. differences the lack of differences is still worth noting. How do these results relate to previous findings on the health beliefs of CAM users and how does the historical context of the current findings compare to findings regarding health beliefs from previous research? Again though no conclusions can be made regarding how such belief differences between groups might “drive” care-seeking as there is compelling evidence to suggest that such beliefs change over the course of CAM treatment.</p>	<p><u>A section has been added to the discussion to highlight CAMBI results and their potential contribution to criterion validity outside the United Kingdom where it was first tested.</u></p>
TABLES	
<p>REV. #1: The Education variable should be presented in three categories (compulsory, middle level and higher education) in table 1.</p>	<p>In France, secondary school is compulsory (<i>lycée</i>). National statistics are dichotomised below secondary school level (compulsory education) and secondary school completed (or above).</p> <p><u>No change suggested.</u></p>

REV. #1: In table 1 , line 19, page 9, there is an error ("48.pe9"). In line 40, 46 and 51 the 31 min, 12+ could be changed to >30 / >12 or over 30/12.	<u>Typo removed and changes made as suggested.</u>
REV. #1: Table 1 could include a column with p-values	As tables 1 and 2 are already quite loaded, we feel that a superscript to indicate statistical significance is sufficient. <u>No change suggested – please advise otherwise.</u>
REFERENCES	
REV. #1: The references from 12 and onwards is wrongly numbered in the text, starting with line 43 on page 6.	<u>Thank you - References have been checked and renumbered.</u>

STROBE Statement—Checklist (cross-sectional studies): ‘What drives patients with sleep, anxiety or depressive disorders to seek care from general practitioners with preference for homeopathy and other complementary medicines? Results from the EPI3 population survey’ by Lamiae Grimaldi-Bensouda et al.

	Item No	Recommendation	
Title and abstract	1	(a) Indicate the study’s design with a commonly used term in the title or the abstract	✓
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	✓
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	✓
Objectives	3	State specific objectives, including any prespecified hypotheses	✓
Methods			
Study design	4	Present key elements of study design early in the paper	✓
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	✓
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants	✓
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	✓
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	✓
Bias	9	Describe any efforts to address potential sources of bias	✓
Study size	10	Explain how the study size was arrived at	✓
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	✓
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	✓
		(b) Describe any methods used to examine subgroups and interactions	✓
		(c) Explain how missing data were addressed	N/A
		(d) If applicable, describe analytical methods taking account of sampling strategy	N/A
		(e) Describe any sensitivity analyses	N/A
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	✓
		(b) Give reasons for non-participation at each stage	✓
		(c) Consider use of a flow diagram	N/A
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	✓
		(b) Indicate number of participants with missing data for each variable of interest	N/A
Outcome data	15*	Report numbers of outcome events or summary measures	✓
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted	N/A

		estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	
		(b) Report category boundaries when continuous variables were categorized	N/A
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	N/A
Discussion			
Key results	18	Summarise key results with reference to study objectives	✓
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	✓
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	✓
Generalisability	21	Discuss the generalisability (external validity) of the study results	✓
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	✓

Symbols: ✓, checked; N/A, not applicable.

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.



Who seeks primary care for sleep, anxiety and depressive disorders from physicians prescribing homeopathic and other complementary medicine? Results from the EPI3 population survey.



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Who seeks primary care for sleep, anxiety and depressive disorders from physicians prescribing homeopathic and other complementary medicine? Results from the EPI3 population survey.

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2
3 **Abstract**
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7 **Objectives:** To describe and compare patients seeking treatment for sleep, anxiety and depressive
8 disorders (SADD) from physicians in general practice (GPs) with three different practice preferences:
9 strictly conventional medicine (GP-CM), mixed complementary and conventional medicine (GP-Mx),
10 and certified homeopathic physicians (GP-Ho).
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15 **Design and setting:** The EPI3 survey was a nationwide, observational study of a representative
16 sample of general practitioners and their patients, conducted in France between March 2007 and
17 July 2008.
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21 **Participants:** 1572 patients diagnosed with SADD.
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24 **Primary and secondary outcomes:** Patients' attitude towards complementary and alternative
25 medicine (CAM); psychotropic drug utilisation.
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28 **Results:** Compared to patients attending GP-CM, GP-Ho patients had healthier lifestyles whilst GP-
29 Mx patients showed similar profiles. Psychotropic drugs were more likely to be prescribed by GP-CM
30 (64%) than GP-Mx (55.4%) and GP-Ho (31.2%). The three groups of patients shared similar SADD
31 severity.
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36 **Conclusion:** Our results showed that patients with SADD, whilst differing principally in their socio-
37 demographic profiles and conventional psychotropic prescriptions, were actually rather similar
38 regarding the severity of SADD in terms of comorbidities and QOL. This information may help to
39 better plan resource allocation and management of these common health problems in primary care.
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48 **Article summary**
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51 **Article focus**
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- 53 • Up to 20% of patients attending primary healthcare in developed countries suffer from the
54 often linked anxiety and depression disorders.
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- Conventional treatments, particularly antidepressants and anxiolytics, are widely prescribed; often associated with adverse side effects, conventional treatments are a likely cause for an increasing number of patients to choose homeopathy and other complementary therapies.
- Understanding the characteristics of physicians and patients, prescribing or using homeopathy, respectively, in conjunction with or instead of psychotropic drugs is undoubtedly of clinical and public health relevance.

Key messages

- Our results suggest that patients experiencing SADD who chose a GP with a clear orientation towards homeopathy, differed in their socio-demographic profile but not in the severity of their mental illness from those attending regular GPs with prescribing preferences towards conventional psychotropic drugs.
- Our survey is one the few studies highlighting that sleep, anxiety and depressive disorders show similar burdens in terms of severity and impact on mental impairment regardless of GPs' prescribing preferences.
- Our results showed that patients with SADD, whilst differing principally in their socio-demographic profiles and conventional psychotropic prescriptions, were actually rather similar regarding the severity of SADD in terms of comorbidities and QOL

Strengths and limitations

- Strengths of the EPI-3 study include high representativeness of the patients involved and comparability against other nationwide studies.
- The main limitation of our study relates to the classification of GPs, which relied on self-reporting of complementary and alternative medicine (CAM) prescriptions; generalisations of the results must be therefore made cautiously since our findings relate to general practice in France.

INTRODUCTION

Mental health problems such as sleep, anxiety or depressive disorders (SADD) are responsible for considerable disability worldwide[1] resulting in serious quality of life impairment[2] and are often associated with high use of medical services. It is estimated that up to 20 percent of patients attending primary healthcare in developed countries suffer from the often linked disorders of anxiety and depression. A high prescription rate of conventional therapies, particularly antidepressants,[3,4] which are often associated with adverse side effects, are a likely cause for an increasing number of patients to choose homeopathy and other complementary therapies.[5]

Evidence of effectiveness of these therapies compared to conventional psychotropic drugs is still limited.[6-8] Nonetheless, their perceived safety may be an important factor motivating patients with SADD disorders to seek care from GPs preferring homeopathy and other types of complementary medicine. Among complementary alternative medicine (CAM) modalities of practice, homeopathy is widely used in countries with large access to conventional medicine and represents a particularly good marker for CAM practice in France, where homeopathic drugs are partly reimbursed by national health insurance and prescribed only by a medical practitioner, if not purchased as over-the-counter drugs.[9] In a previous study,[10] homeopathic practitioners (including non-medical healthcare professionals) indicated that their patients used homeopathy mainly in association with conventional psychotropic treatments, psychotherapy and counselling in a mixed practice.

Understanding the characteristics of physicians and patients, prescribing or using homeopathy, respectively, in conjunction with or instead of psychotropic drugs is undoubtedly of clinical and public health relevance. The objective of this study was to describe and compare patients seeking treatment for sleep, anxiety and depressive disorders (SADD) from physicians in general practice

(GPs) with three different practice preferences: strictly conventional medicine (GP-CM), mixed complementary and conventional medicine (GP-Mx), and certified homeopathic physicians (GP-Ho).

METHODS

Study design, settings and participants

The EPI3 survey was a nationwide, observational study of a representative sample of general practitioners and their patients, conducted in France between March 2007 and July 2008. The methodology of the study has been described elsewhere.[2]

Participants (GPs and their patients) were drawn by applying a two-stage sampling process. The GPs were first randomly selected from the French national directory of physicians and invited to participate, which meant allowing a research assistant to conduct a one-day survey in the waiting room at the doctor's practice. Blind to the study focus on conventional and complementary alternative medicine (CAM) practice, consenting GPs were next contacted by telephone to enquire how frequently they prescribed CAM (homeopathy, mesotherapy, acupuncture, phytotherapy, etc.). Depending on their prescribing preferences towards homeopathic medicines, they were classified as: strictly conventional GPs (GP-CM), who declared themselves never or rarely using CAM or homeopathic medicines; mixed practice (GP-Mx), who were GPs declaring using CAM regularly; and GPs certified in homeopathic practice (GP-Ho). In France, homeopathy can only be prescribed by physicians, mostly GPs qualified as homeopaths by the French National Council of Physicians (CNOM) upon completion of specific training and certification (3.3% of all French GPs in 2008).[11]

The second stage of selection consisted of random one-day sampling of consultations per participating physician, in order to survey all patients attending the practice on that very day. All adults (18 years old and over) and accompanied minor patients were eligible for inclusion in the EPI3 survey, except those whose health status or literacy level did not allow responding to a self-administered questionnaire.

During the consultation, GPs asked all adult patients diagnosed or suspected of suffering SADD whether they would volunteer for a more in-depth study of their disease. Consenting patients were contacted again within 72 hours for a telephone interview conducted by trained interviewers.

Data collection

Collection of data from patients included: age, gender, nationality, educational attainment, type of health insurance, additional private insurance, smoking habit, alcohol intake, physical activity, height, weight, employment status, familial status, previous number of visits and referrals to physicians. Participants were also asked to confirm whether the attending GP was their regular primary care physician or not. In France, all citizens are required to choose a GP as their regular physician. This study was based on patients who reported being seen exclusively by their regular family physician. Health-related quality of life was assessed using the validated 12-item Short Form (SF-12) questionnaire,[12] allowing estimation of physical health (PCS score) and mental health (MCS score); the SF-12 questionnaire was validated in the late 90s for use in the US, the UK, France and many other European countries.[13] Patients also completed the Complementary and Alternative Medicine Beliefs Inventory (CAMBI), which assesses attitudes and expectations of patients towards medical care, participation in decision making, perception of risks associated with treatment, and understanding of both illness and healing process via a 17-question inventory.[14] High scores on the CAMBI items indicate pro-CAM treatment belief. GPs recorded the main reason for consultation and up to five other diagnoses present that day as well as their prescriptions, which were entered by the interviewer in a database that automatically recorded the corresponding ATC (Anatomical Therapeutic Chemical) codes, revision 2009. Diagnoses relating to 100 diseases[2] were coded by a trained archivist using the 9th revision of the International Classification of Diseases.[15] Patients with the following ICD codes were classified as anxious: 300.0 anxiety states; 300.2 phobic disorders; 300.3 obsessive-compulsive disorders; 300.5 neurasthenia; 300.8 somatoform disorders; 306.2 psychogenic disease related to underlying physiological disorders. Patients with the following ICD codes were classified as depressive: 296.3

major depressive disorder, recurrent episode; 296.5 bipolar disorder, most recent episode depressed; 296.1 manic disorder; 296.6 manic-depressive psychosis; 300.4 dysthymic disorders; 300.5: neurasthenia; 309.0 adjustment reaction, 309.1 prolonged depressive reaction, 311.9 unclassified depressive disorders. Patients were considered as experiencing sleep disorders if their diagnoses related to ICD codes 307.4 (specific disorders of sleep of non-organic origin) and 780.5 (sleep disturbances).

Comorbidity was defined as the presence of at least one diagnosis other than the principal motive for consultation at the recruitment visit. Comorbidities were categorised as: co-associated sleep, anxiety, or depressive disorder (other than the main reason for consultation), musculoskeletal disorders, respiratory diseases, cardiovascular and metabolism disorders, diabetes, thyroid and endocrine disorders, and finally digestive disorders. Severity of SADD was characterised firstly by degree of quality of life (QoL) impairment, then by the presence and finally by number of associated comorbidities.

Statistical analysis

Characteristics of non-participants (age, gender, length of time attending the GP's medical practice, type of health insurance and main reasons for consultation) were used to calibrate the final sample as previously reported[2] to ensure that it would closely represent the whole population attending French GPs practices, using a method known in demographic studies as the CALMAR procedure.[16] Overall characteristics of patients seeking access to each of the three types of GP and results reported here were based on weighted data. Distributions were compared using Chi-Square and Fisher tests for categorical variables and Student and Wilcoxon tests for continuous variables.

Multiple logistic regression analyses were used to compare patients in the GP-CM group to GP-Mx and GP-Ho groups for categorical variables and were adjusted for all variables listed in Table 1 to control for potential confounding.

The GP-Mx and GP-Ho groups were compared to the GP-CM group for patients' exposure to antidepressants (ATC codes beginning with N06AB, N06AX, N06AA and N06AF), anxiolytics and hypnotics (ATC codes beginning with N05BA, N05BB, N05BX, N05BE, N05CD, N05CF and N03AE) mood normalisers (N05AN, N03AG) and antipsychotics (ATC codes beginning with N05AK, N05AA, N05AB, N05AC, N05AD, N05AF, N05AG, N05AH, N05AL, N05AX, N07XX) as well as homeopathic preparations specifically prescribed for SADD symptoms.

ANCOVA analyses were performed to provide mean scores for the SF-12 mental (MCS) and physical scales (PCS) adjusted for age (<40, 40-60, 60+ years), gender, marital status, employment status, body mass index (BMI), number of associated comorbidities (other than SADD), and finally associated SADD (other than the main diagnose, yes/no). MCS score and PCS score were categorised into quartiles corresponding to: 34.1 (Q1), 42.4 (Q2), and 48 (Q3) for MCS; 39.3 (Q1), 47.3 (Q2) and 54.2 (Q3) for PCS.

Associations between scores from each of the 17 questions of the CAMBI questionnaire and the probability of attending a GP-Mx or GP-Ho as compared to a GP-CM were computed after adjusting for age, gender and educational level. Scores obtained per question, ranging from 1 (totally disagree) to 7 (totally agree), were dichotomised in order to further distinguish participants clearly in favour (scoring 5 to 7) or in disagreement (scoring 1 to 3) with the 17 CAMBI questions. Each of the three subscales scores and the total CAMBI score were then dichotomised according to the 75th percentile (40, 26 and 33, respectively; 96 for the total score).

The possibility of a clustering effect at the practice level was tested using Generalised Estimating Equations (GEE) multivariate models. All the analyses were performed with SAS software version 9.1 (SAS Institute, Inc., Cary, North Carolina).

The study was approved by the French National Data-Protection Commission (CNIL) and the CNOM. Participating physicians received compensation fees for recruiting patients but not patients.

RESULTS

A total of 825 GPs participated in the survey. There was no difference between the three groups of GPs for age (mean = 50.7 years) but GP-Ho and GP-Mx were more often women than GP-CM (48.9% and 31.5% versus 20.3%, respectively), and less often salaried (14.3% and 16.9% versus 34.5%, respectively). In addition, GP-Ho were more likely to practise alone than GP-CM and GP-Mx (72.4% versus 51.8% and 55.9%, respectively) (all differences statistically significant). Among the 11 701 patients attending the doctor's office on the survey day, 8652 (73.9%) agreed to participate and complete information was collected for 8559 (73.1%) patients. Compared to non-participants, participants were more often women (62.7% and 56.8%, respectively), younger (mean age 43.3 and 47.7, respectively) and more likely to consult for a SADD (20.6% and 11.6%, respectively). Of the 6379 who declared the consulting physician as their regular GP, 1572 met the inclusion criteria and were included in the analyses with the following diagnoses: anxiety (n=370), depression (n=583), sleep disorders (n=480) or SADD of undetermined cause (n=139).

Compared to the GP-CM group, patients from the GP-Mx group showed similar characteristics but those from the GP-Ho group were more frequently younger, more educated, employed women living with children or a spouse (Table 1). They also had a healthier lifestyle with lower BMI, and were more frequently non-smokers and occasional or non-consumers of alcohol. They declared however less visits to their regular GP in the previous year. Motives of consultation showed more anxiety and less depression in the GP-Ho group than in the two others but the distribution was unremarkable otherwise. Physicians prescribing preferences were confirmed with the GP-Ho group using more homeopathy and less psychotropic drugs than the two other groups. The GP-Mx group however did not differ much from the GP-CM group.

Table 1. Characteristics of patients seeking care for SADD according to the type of practice of their regular GP (EPI3 Survey, n=1572)

	GP-CM (n=410) N, weighted %	GP-Mx (n=718) N, weighted %	GP-Ho (n=444) N, weighted %
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Gender						
Females vs. Males	269	64.7	500	68.9	323	72.6*
Age categories (years)						
18-39	92	20.7	195	26.7	131	28.8*
40-59	163	38.9	298	41.3	193	43.6*
60 and over	155	40.4	225	32.0	120	27.6*
Employment status						
Employed	171	39.5	353	48.9	240	53.5*
Educational level						
Secondary school not completed	93	22.1	177	22.9	158	35.2*
Universal Health Insurance coverage (CMU)						
	36	9.5	65	9.8	26	6.5
Familial status						
Living with children	164	38.1	306	42.5	195	44.1*
Living with a spouse	239	56.6	439	61.2	285	64.0*
Body Mass Index (%)						
<25	216	52.1	413	57.9	302	67.9*
25-30	124	30.9	186	25.6	106	24.0*
>30	70	17.0	119	16.6	36	8.1*
Tobacco consumption (%)						
Never smoked	195	48.4	365	50.8	251	57.1*
Past smoker	111	26.9	170	23.6	112	24.6*
Current smoker	104	24.8	183	25.6	81	18.3*
Alcohol Consumption (%)						
Never	152	37.4	287	40.0	142	32.4
Sometimes	193	46.4	354	49.3	254	56.2
Daily	65	16.3	77	10.7	48	11.4
Physical exercise (%)						
> 30 minutes / day	125	30.7	207	29.3	140	31.6
Number of visits to regular GP during the last year						
None	7	1.7	16	2.3	10	2.2
1-6	228	55.4	405	57.0	296	66.8*
7-12	142	34.6	234	32.1	114	25.6*
12 and over	33	8.4	63	8.7	24	5.4*
Number of visits to a specialist during the last year						
None	105	25.8	200	28.0	113	25.6
1	114	27.0	206	28.6	137	31.2
2	63	15.6	133	18.4	82	18.1
2+	128	31.5	179	25.0	112	25.1
Motive for consultation (ICD-9)						
Anxiety	79	18.8	158	21.2	133	30.2*
Depression	171	41.1	284	39.6	127	28.7*
Sleep disorders	131	32.7	198	28.9	151	34.0
Unspecified	52	12.6	95	12.5	65	14.1
Treatment						
Any psychotropic drugs	266	64.0	404	55.4	138	31.2*
<i>Antidepressants</i>	152	36.0	231	31.5	73	16.5*
<i>Anxiolytics/hypnotics</i>	185	44.8	286	39.3	87	19.8*
<i>Antipsychotics</i>	11	3.1	25	3.5	10	2.4
<i>Normothymics</i>	16	3.9	7	1.1	20	4.6
Other conventional drugs	144	36.0	289	41.2	189	42.7
Homeopathic medicines for SADD	1	0.2	36	4.9	139	30.9*
Other homeopathic medicines	6	1.4	58	7.8	288	67.7*

Abbreviations: GP-CM: general practitioner strictly practising conventional medicine; GP-Mx: general practitioner with mixed practice; GP-Ho: general practitioner with a certification in homeopathic care.

*Difference with conventional medicine category statistically significant ($p \leq 0.05$) in logistic regression including all variables.

Considering the severity of mental health problem, the GP-Mx group had systematically less often an associated SADD comorbidity than in the two other groups but the distribution of comorbidities other than SADD was unremarkable otherwise between groups (Table 2). For quality of life, the mental score summary (MCS) of the SF-12 was similar across the three groups with no clinically or statistically meaningful difference (Table 3). The GP-Ho group however had a slightly better physical summary score (PCS) than the two other groups.

Table 2. Burden of associated comorbidity and other psychological distress in patients with sleep, anxiety, or depressive disorders according to the type of practice of regular GPs (EPI3 Survey, n=1572)

Comorbidities present at the medical visit	GP-CM Weighted%	GP-Mx Weighted%	Gp-Ho Weighted%
Patients with SADD (n=1572)*	n=410	n=718	n=444
Associated SADD comorbidity (other than primary)	7.4	2.6 ⁺	5.3
At least one other comorbidity	74.3	68.7	69.5
MSD	27.1	23.8	24.8
Respiratory diseases	16.6	11.7	18.5
Cardiovascular and metabolism disorders	35.1	30.2	22.9 ⁺
Diabetes, thyroid and endocrine disorders	12.7	9.6	8.1
Digestive disorders	11.9	11.5	11.5
Patients with depression (n=583)	n=171	n=285	n=127
Associated SADD comorbidity (other than depression)	13.7	3.7 ⁺	10.0
At least one other comorbidity	75.2	67.3 ⁺	70.6 ⁺
MSD	29.2	23.2	28.6
Respiratory diseases	15.3	9.8 ⁺	12.8
Cardiovascular and metabolism disorders	36.5	30.4	21.6 ⁺
Diabetes, thyroid and endocrine disorders	13.0	10.8	7.9 ⁺
Digestive disorders	10.4	9.0	10.6
Patients with anxiety (n=370)	n=79	n=158	n=133
Associated SADD comorbidity (other than anxiety)	12.9	5.7 ⁺	13.6
At least one other comorbidity	71.2	72.2	62.2 ⁺
MSD	22.5	26.5	25.2
Respiratory diseases	14.3	9.8	14.2
Cardiovascular and metabolism disorders	23.6	31.2 ⁺	22.3

<i>Diabetes, thyroid and endocrine disorders</i>	10.7	11.7	9.3
<i>Digestive disorders</i>	18.1	15.0	13.7
Patients with sleep disorder (n=480)	n=131	n=198	n=151
Associated SADD comorbidity (other than sleep disorder)	9.8	3.7	9.7
At least one other comorbidity	71.3	63.6	67.6
<i>MSD</i>	29.7	22.0	21.9 ⁺
<i>Respiratory diseases</i>	14.3	12.7	21.2
<i>CV and metabolism disorders</i>	37.8	28.9	19.4
<i>Diabetes, thyroid and endocrine disorders</i>	10.4	5.6 ⁺	4.4 ⁺
<i>Digestive disorders</i>	10.2	10.7	12.1

Abbreviations: GP-CM: general practitioner strictly practising conventional medicine; GP-Mx: general practitioner with mixed practice; GP-Ho: general practitioner with a certification in homeopathic care; MSD: musculoskeletal disorders; SADD: sleep, anxiety or depressive disorders.

*Including missing diagnosis (according to ICD9) values (n=139 patients).

+Difference with conventional medicine category statistically significant ($p \leq 0.05$) in logistic regression including age (<40, 40-60, 60+ years), gender, marital status, employment status, BMI (body mass index: <25; 25-30; >30kg/m²), MCS: SF12-Mental Component Summary score; PCS: SF12-Physical Component Summary score.

Table 3. Adjusted quality of life (MCS and PCS) of patients visiting their regular GP according to the type of practice (EPI3 Survey, n=1572)

Quality of Life SF-12		GP-CM Mean (sd)*	GP-Mx Mean (sd)*	p-value*	GP-Ho Mean (sd)*	p-value*
SADD						
	MCS	35.3 (1.0)	35.9 (1.0)	0.64	36.4 (1.0)	0.24
	PCS	42.3 (1.0)	42.9 (1.0)	0.58	45.4 (1.0)	<0.001
Anxiety						
	MCS	36.7 (1.4)	35.8 (1.2)	0.73	37.3 (1.2)	0.88
	PCS	44.1 (1.4)	44.8 (1.2)	0.81	47.4 (1.3)	0.03
Depression						
	MCS	34.5 (1.4)	34.6 (1.5)	0.99	34.0 (1.6)	0.92
	PCS	40.5 (1.5)	41.9 (1.5)	0.29	44.1 (1.6)	0.006
Sleep disorders						
	MCS	34.6 (1.6)	37.0 (1.6)	0.06	35.7 (1.7)	0.64
	PCS	44.4 (1.6)	44.3 (1.7)	0.99	47.5 (1.7)	0.03

Abbreviations: GP-CM: general practitioner strictly practising conventional medicine; GP-Mx: general practitioner with mixed practice; GP-Ho: general practitioner with a certification in homeopathic care; MSD: musculoskeletal disorders; MCS: SF12-mental component summary score; PCS: SF12-physical component summary score SADD: sleep, anxiety or depressive disorders.

*from ANCOVA adjusted for age (<40, 40-60, 60+ years), gender, marital status, employment status, BMI, number of associated comorbidities (other than main SADD), SADD comorbidity (yes/no); a higher score indicates better health.

The attitudes towards complementary medicine estimated by CAMBI (Table 4) showed that patients in the GP-Ho group had a probability of scoring high (favourable to CAM) over three times that of the GP-CM group (Odds ratio (OR) = 3.65, 95% confidence interval (CI): 2.94-3.77). The result was consistent for each of the three CAMBI subscales with OR= 2.08 (95% CI: 1.78-2.32) for belief in natural treatment, OR= 1.43 (95% CI: 1.23-1.77) for active patient's participation in care, and OR= 2.75 (95% CI: 2.55-3.24) belief in holistic medicine. CAMBI scores from patients of the GP-Mx group were comparable to the GP-CM group, although a slightly higher trust in natural treatment subscale was observed (OR = 1.15, 95% CI: 1.03-1.26).

Table 4. Attitudes of patients with SADD towards complementary medicine as measured by the CAMBI (attitudes towards complementary and alternative medicine beliefs inventory) questionnaire (EPI3 Survey, n=1572)

	Type of practice	
	GP-Mx vs. GP-CM OR* (95% CI)	GP-Ho vs. GP-CM OR* (95% CI)
1. Treatments should have no negative side effects	1.11 (0.94-1.33)	1.70 (1.43-1.93)
2. It is important to me that treatments are not toxic	0.85 (0.65-1.14)	1.55 (1.41-2.03)
3. Treatments should only use natural ingredients	1.07 (0.97-1.08)	2.02 (1.87-2.47)
4. It is important that treatments boost my immune system	1.12 (0.93-1.18)	1.65 (1.38-2.11)
5. Treatments should allow my body to heal itself	1.28 (1.13-1.38)	2.02 (1.77-2.18)
6. Treatments should increase my natural ability to keep healthy	1.05 (1.01-1.34)	1.54 (1.64-2.27)
7. Treatment providers should treat patients as equals	1.01 (0.89-1.17)	1.24 (1.08-1.67)
8. Patients should take an active role in their treatment	0.88 (0.81-1.06)	1.75 (1.18-1.81)
9. Treatment providers should make all decisions about treatment	0.85 (0.74-1.07)	1.37 (1.21-1.54)
10. Treatment providers should help patients make their own decisions about treatment	0.94 (0.86-1.11)	2.43 (1.89-2.43)
11. Treatment providers control what is discussed during consultations	1.04 (0.85-1.19)	1.37 (1.18-1.45)
12. Health is about harmonising your body, mind and spirit	1.08 (0.95-1.20)	2.33 (1.55-2.45)
13. Imbalances in people's lives are a major cause of illness	1.15 (1.02-1.27)	2.07 (1.66-2.07)

14. Treatments should focus only on symptoms rather than the whole person	0.82 (0.78-1.04)	2.44 (1.75-2.45)
15. Treatments should focus on people’s overall well-being	1.21 (1.01-1.44)	1.53 (1.48-1.95)
16. I think my body has a natural ability to heal itself	1.13 (0.95-1.22)	2.43 (1.70-2.22)
17. There is no need for treatments to be associated to natural healing power	1.00 (0.77-1.07)	1.56 (1.33-1.81)
CAMBI Total score >Q3	1.05 (0.92-1.29)	3.65 (2.94-3.77)
CAMBI sub-scores:		
• Natural treatment >Q3	1.15 (1.03-1.26)	2.08 (1.78-2.32)
• Patient’s participation >Q3	0.95 (0.81-1.03)	1.43 (1.23-1.77)
• Holistic medicine >Q3	1.15 (0.95-1.17)	2.75 (2.55-3.24)

Abbreviations: GP-CM: general practitioner strictly practising conventional medicine; GP-Mx: general practitioner with mixed practice; GP-Ho: general practitioner with a certification in homeopathic care; OR: Odds ratio

*adjusted for age, gender and educational level.

DISCUSSION

To our knowledge, the EPI3 study is the first nationwide survey conducted in a large representative sample of patients to provide characteristics and attitudes, as well as the first to quantify quality of life and the burden of sleep, anxiety or depressive disorders (SADD) in patients seeking care from their regular GPs with different preferences towards CAM and homeopathic practices.

Our results suggest that patients experiencing SADD, and who chose a GP with a clear orientation towards homeopathy, differed in their socio-demographic profile but not in the severity of their mental illness from those attending regular GPs with prescribing preferences towards conventional psychotropic drugs. Patients with SADD attending a GP-Ho in our study were more likely to be female, as previously reported[17-20] except for one survey,[21] and younger. Association with age been suggested by other authors,[22] although no such association has been described elsewhere.[17,19,21]

Patients seeking care from a GP-Ho and to a lesser extent from GP-Mx, had healthier lifestyles as shown by a lower BMI and the higher number of patients that never smoked in this group, a finding that has been noted previously.[23] Greater health awareness might not only be a driver for

consulting a CAM provider but also for changing from a GP-CM because of dissatisfaction with care.[24] In these circumstances, health awareness might be a proxy variable to several other motivations including a desire for shared decision making.[25] As noted by other authors, the directionality of the relation between healthy lifestyle and consulting a GP-Ho could go in the opposite direction, with CAM utilisation [26] and interaction with a CAM practitioner [27] promoting a healthier lifestyle. More longitudinal research is needed to clarify these associations. The higher educational attainment found among patients seeking mixed and homeopathic GPs has also been previously reported in some studies [17,19] but not in others.[20,21] More educated people may be more knowledgeable about the side effects of conventional psychotropic drugs and hence more likely to seek alternative treatments as suggested by Mac Lennan et al.[18]

With regard to the medical conditions, the EPI3 survey is one of the few studies highlighting that sleep, anxiety and depressive disorders show similar burdens in terms of severity and impact on mental impairment regardless of practice modalities of GPs. As for prevalence, anxiety was confirmed as the most frequent mental health disorder encountered by alternative medicine practitioners, as previously reported.[5,10] Higher prevalence of patients suffering from depression seeking GP-CM might be attributed to the older age structure observed in this group when compared to those consulting GP-Ho: age trajectories observed for depression are often the opposite as those found for anxiety.[28] In spite of the fact that patients with depressive disorders in our study were less likely to seek strictly homeopaths than GP-CM, we must remember that depression is also one of the most commonly treated complaints as previously described for outpatient clinics of homeopathic hospitals in the UK National Health Service.[29]

Studies examining representative samples of general population seeking care for SADD have consistently shown that a large proportion of subjects are not treated with psychotropic drugs.[30,31] Conversely, psychotropic drugs use is frequently reported by subjects without identified psychiatric disorders.[32] This latter observation is probably the reason why there is an

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2
3 increasing trend for patients falling into the mixed category with similar characteristics and SADD. It
4
5 is as if they sought a combination of both homeopathy and conventional medicines to fulfil
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7 individualised and holistic therapies needs and expectations, whilst being sure that good standards of
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9 medical and scientific practice were met.[33] This type of patients seems to be primarily concerned
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11 by associating their need for care and adequate treatment. One third of the patients with SADD
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13 consulting a GP-Mx received concomitantly homeopathic medicines and a psychotropic drug: this
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15 might suggest that homeopathic medicines could be prescribed not only as a substitute of
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17 unnecessary conventional psychotropic drugs, but also viewed as an adjunct to efficient psychotropic
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19 drugs;[10,20,34] such combination has been found to potentially help patients to accept and
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21 improve their symptoms[35] whilst avoiding some possible side effects of additional conventional
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23 therapies. Although no conclusions can be drawn at this stage on the outcome of consultations to
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25 GP-Mx and GP-Ho and whether their patients were given adequate treatment, our study highlights a
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27 genuine will from GP-Mx and GP-Ho to tailor therapies to their patients while avoiding unnecessary
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29 prescriptions.
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33 High CAMBI scores, representing greater trust and belief in CAM, were found in the GP-Ho group,
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35 particularly in the subscales related to belief in natural treatments and holistic medicine and to a
36
37 lesser degree in the patient's participation subscale. Patients of the GP-Mx group exhibited only a
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39 modest preference for natural treatments and holistic medicine with no difference overall towards
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41 patients seen by physicians who practise strictly conventional medicine. The different findings might
42
43 be explained by the fact that GP-Ho operate a labelled practice in France (they must be certified
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45 homeopaths) which is not the case for the GP-Mx group defined specifically for this study. Our results
46
47 provide interesting evidence of criterion validity for the CAMBI scale outside the United Kingdom. As
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49 for the quality of life scale (SF-12), patients scored similarly on the mental health subscale across all
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51 three groups of GPs, a result that was consistent with the similar number of comorbidities declared
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53 by treating physicians. Some studies found that patients seeking CAM therapies showed more QoL
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55 impairment than patients seeking conventional therapies.[36] Other studies, including ours, suggest
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that, despite the modality of practice (CAM or conventional therapies), GPs treat patients exhibiting similar mental health problems and disease burden.[37]

Around 75% of patients who sought GPs exhibited additional morbidities in the EPI3 survey. The role of comorbidity in producing further burden from sleep, anxiety and depressive disorders has not been studied in patients attending GPs practising different modalities of treatment.[38,39]

Integrating research to understand the role of comorbidity in QoL is challenging due to differences across studies in QoL conceptualisation, validity of QoL measurement, recruitment context (e.g., epidemiological, treatment-seeking), and consideration of socio-demographic and clinical predictors. Studies generally account for a limited range of comorbidity attributes, typically the presence versus absence of comorbidity, which loses the richness of information inherent in psychiatric presentations.

Together with a lower number of visits to GPs and a lower proportion of prescribed psychotropic drugs in the GP-Ho group, our findings may have relevant public health implications. For instance, the National Institute for Health and Clinical Excellence (NICE), highlighted recently that the severity of depression at which antidepressants show consistent benefits over placebo is poorly defined, emphasising that, in general, the more severe the symptoms, the greater the benefit.[40] A patient-level meta-analysis demonstrated a lack of efficacy for antidepressants in the majority of patients with anxiety and depressive disorders.[3,4] Thus, the real impact of conventional antidepressants in this population is considerable, with adverse reactions outweighing potential benefits.[41] The patient's dissatisfaction with psychotropic drugs is one of the reasons cited for seeking other treatment options[42] and patients with a history of depression are more likely to seek CAM than those who have never been depressed before.[43]

Under a primary care system designed for acute rather than chronic care, where clinicians "routinely experience the tyranny of the urgent", [44] our results suggested that management of SADD by GP-Ho was associated with less visits to the GP in the previous year but no more consultations to specialists than GP-CM. Medico-economic studies are needed to assess the patterns of access to and

management by these different practitioners, which would contribute to better plan resource allocation for mental health services and target key groups for interventions in prevention, as far as severity of SADD is concerned.

Strengths and limitations of the study

The present study examined a relatively large number of primary care practices in order to provide a real-world picture of CAM and homeopathic practice within the French primary care setting. The main strengths of the EPI3 survey have already been acknowledged elsewhere.[2] These include high representativeness of the patients involved and comparability against other nationwide studies. The weighted geographical distribution of the participating GPs in the survey was similar to the national distribution of GPs in private practice across the 22 French regions surveyed, and the distribution of physicians’ individual characteristics regarding age, gender, type of contract with national health insurance and modality of practice differed only slightly from national statistics.[45]

The main limitation of our study relates to its cross-sectional design which does not allow addressing the directionality of the associations described between patients’ characteristics and their physician’s choice of medical practice. Another limitation relates to the classification of GPs, which relied on self-reporting of CAM prescriptions. The definition of GP-Ho was more accurate and based on their professional certification. Therefore, generalisations of the results must be made cautiously, since our findings represented general practice in France. Nevertheless, this particular setting can be otherwise interpreted also as a strength, because it provided a unique opportunity to compare head-to-head primary care practices differing only by preferences for homeopathy and CAM, whereas all participant physicians shared similar medical professional status and basic training in conventional medicine. We feel that albeit the context of the study was specific to one country, differences between the groups of patients provided reliable information on the differential utilisation of homeopathy and CAM.

Finally, the fact that the participants were recruited in primary care might have excluded people with severe psychiatric disorders. This potential bias was likely to underestimate the prevalence of

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3 psychotropic drug use. However, prescriptions for psychotropic drugs were similar to those found in
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5 other French studies.[46,47]
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7 8 **CONCLUSION**

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10 The EPI3 survey is one of the largest studies to date conducted in general practice to describe
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12 attitudes and burden of sleep, anxiety and depressive disorders in patients seeking care from GPs
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14 with different prescribing preferences towards CAM and homeopathic practices. Our results showed
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16 that patients with SADD, while differing principally in their socio-demographic profiles and
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18 conventional psychotropic prescriptions, were actually rather similar regarding the severity of SADD
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20 in terms of comorbidities and QOL. Further research is needed to explore potential benefits, both in
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22 terms of health economics and care, of consulting GPs that combine CAM and CM daily in the clinical
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24 management of SADD.
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14 **Competing interests**
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16
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32 **Contributors**
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37 DG, BA, GD, A-MM, MR and LA conceived both the research theme and the methods, analysed the
38
39 data and interpreted the results. LG-B implemented the trial in France, analysed the data, and
40
41 together with FL, PE and LA drafted and revised the paper. All members of the EPI3-LA-SER group
42
43 designed the study. A Fabre and PE analysed the data. All authors have contributed to, read and
44
45 approved the final manuscript. LG-B is guarantor for the study. LG-B, PE and LA had full access to all
46
47 of the data in the study and take responsibility for the integrity of the data and the accuracy of the
48
49 data analysis.
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54 **Data sharing statement**
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56 No additional data available.
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Who seeks primary care for sleep, anxiety and depressive disorders from physicians prescribing homeopathic and other complementary medicine? Results from the EPI3 population survey.

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3 **Abstract**
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7 **Objectives:** To describe and compare patients seeking treatment for sleep, anxiety and depressive
8 disorders (SADD) from physicians in general practice (GPs) with three different practice preferences:
9 strictly conventional medicine (GP-CM), mixed complementary and conventional medicine (GP-Mx),
10 and certified homeopathic physicians (GP-Ho).
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15 **Design and setting:** The EPI3 survey was a nationwide, observational study of a representative
16 sample of general practitioners and their patients, conducted in France between March 2007 and
17 July 2008.
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22 **Participants:** 1572 patients diagnosed with SADD.
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24 **Primary and secondary outcomes:** Patients' attitude towards complementary and alternative
25 medicine (CAM); psychotropic drug utilisation.
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28 **Results:** Compared to patients attending GP-CM, GP-Ho patients had healthier lifestyles whilst GP-
29 Mx patients showed similar profiles. Psychotropic drugs were more likely to be prescribed by GP-CM
30 (64%) than GP-Mx (55.4%) and GP-Ho (31.2%). The three groups of patients shared similar SADD
31 severity.
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37 **Conclusion:** Our results showed that patients with SADD, whilst differing principally in their socio-
38 demographic profiles and conventional psychotropic prescriptions, were actually rather similar
39 regarding the severity of SADD in terms of comorbidities and QOL. This information may help to
40 better plan resource allocation and management of these common health problems in primary care.
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48 **Article summary**
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51 **Article focus**
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- 53 • Up to 20% of patients attending primary healthcare in developed countries suffer from the
54 often linked anxiety and depression disorders.
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- Conventional treatments, particularly antidepressants and anxiolytics, are widely prescribed; often associated with adverse side effects, conventional treatments are a likely cause for an increasing number of patients to choose homeopathy and other complementary therapies.
- Understanding the characteristics of physicians and patients, prescribing or using homeopathy, respectively, in conjunction with or instead of psychotropic drugs is undoubtedly of clinical and public health relevance.

Key messages

- Our results suggest that patients experiencing SADD who chose a GP with a clear orientation towards homeopathy, differed in their socio-demographic profile but not in the severity of their mental illness from those attending regular GPs with prescribing preferences towards conventional psychotropic drugs.
- Our survey is one the few studies highlighting that sleep, anxiety and depressive disorders show similar burdens in terms of severity and impact on mental impairment regardless of GPs' prescribing preferences.
- Our results showed that patients with SADD, whilst differing principally in their socio-demographic profiles and conventional psychotropic prescriptions, were actually rather similar regarding the severity of SADD in terms of comorbidities and QOL

Strengths and limitations

- Strengths of the EPI-3 study include high representativeness of the patients involved and comparability against other nationwide studies.
- The main limitation of our study relates to the classification of GPs, which relied on self-reporting of complementary and alternative medicine (CAM) prescriptions; generalisations of the results must be therefore made cautiously since our findings relate to general practice in France.

INTRODUCTION

Mental health problems such as sleep, anxiety or depressive disorders (SADD) are responsible for considerable disability worldwide[1] resulting in serious quality of life impairment[2] and are often associated with high use of medical services. It is estimated that up to 20 percent of patients attending primary healthcare in developed countries suffer from the often linked disorders of anxiety and depression. A high prescription rate of conventional therapies, particularly antidepressants,[3,4] which are often associated with adverse side effects, are a likely cause for an increasing number of patients to choose homeopathy and other complementary therapies.[5]

Evidence of effectiveness of these therapies compared to conventional psychotropic drugs is still limited.[6-8] Nonetheless, their perceived safety may be an important factor motivating patients with SADD disorders to seek care from GPs preferring homeopathy and other types of complementary medicine. Among complementary alternative medicine (CAM) modalities of practice, homeopathy is widely used in countries with large access to conventional medicine and represents a particularly good marker for CAM practice in France, where homeopathic drugs are partly reimbursed by national health insurance and prescribed only by a medical practitioner, if not purchased as over-the-counter drugs.[9] In a previous study,[10] homeopathic practitioners (including non-medical healthcare professionals) indicated that their patients used homeopathy mainly in association with conventional psychotropic treatments, psychotherapy and counselling in a mixed practice.

Understanding the characteristics of physicians and patients, prescribing or using homeopathy, respectively, in conjunction with or instead of psychotropic drugs is undoubtedly of clinical and public health relevance. The objective of this study was to describe and compare patients seeking treatment for sleep, anxiety and depressive disorders (SADD) from physicians in general practice

(GPs) with three different practice preferences: strictly conventional medicine (GP-CM), mixed complementary and conventional medicine (GP-Mx), and certified homeopathic physicians (GP-Ho).

METHODS

Study design, settings and participants

The EPI3 survey was a nationwide, observational study of a representative sample of general practitioners and their patients, conducted in France between March 2007 and July 2008. The methodology of the study has been described elsewhere.[2]

Participants (GPs and their patients) were drawn by applying a two-stage sampling process. The GPs were first randomly selected from the French national directory of physicians and invited to participate, which meant allowing a research assistant to conduct a one-day survey in the waiting room at the doctor's practice. Blind to the study focus on conventional and complementary alternative medicine (CAM) practice, consenting GPs were next contacted by telephone to enquire how frequently they prescribed CAM (homeopathy, mesotherapy, acupuncture, phytotherapy, etc.). Depending on their prescribing preferences towards homeopathic medicines, they were classified as: strictly conventional GPs (GP-CM), who declared themselves never or rarely using CAM or homeopathic medicines; mixed practice (GP-Mx), who were GPs declaring using CAM regularly; and GPs certified in homeopathic practice (GP-Ho). In France, homeopathy can only be prescribed by physicians, mostly GPs qualified as homeopaths by the French National Council of Physicians (CNOM) upon completion of specific training and certification (3.3% of all French GPs in 2008).[11]

The second stage of selection consisted of random one-day sampling of consultations per participating physician, in order to survey all patients attending the practice on that very day. All adults (18 years old and over) and accompanied minor patients were eligible for inclusion in the EPI3 survey, except those whose health status or literacy level did not allow responding to a self-administered questionnaire.

During the consultation, GPs asked all adult patients diagnosed or suspected of suffering SADD whether they would volunteer for a more in-depth study of their disease. Consenting patients were contacted again within 72 hours for a telephone interview conducted by trained interviewers.

Data collection

Collection of data from patients included: age, gender, nationality, educational attainment, type of health insurance, additional private insurance, smoking habit, alcohol intake, physical activity, height, weight, employment status, familial status, previous number of visits and referrals to physicians. Participants were also asked to confirm whether the attending GP was their regular primary care physician or not. In France, all citizens are required to choose a GP as their regular physician. This study was based on patients who reported being seen exclusively by their regular family physician. Health-related quality of life was assessed using the validated 12-item Short Form (SF-12) questionnaire,[12] allowing estimation of physical health (PCS score) and mental health (MCS score); the SF-12 questionnaire was validated in the late 90s for use in the US, the UK, France and many other European countries.[13] Patients also completed the Complementary and Alternative Medicine Beliefs Inventory (CAMBI), which assesses attitudes and expectations of patients towards medical care, participation in decision making, perception of risks associated with treatment, and understanding of both illness and healing process via a 17-question inventory.[14] High scores on the CAMBI items indicate pro-CAM treatment belief. GPs recorded the main reason for consultation and up to five other diagnoses present that day as well as their prescriptions, which were entered by the interviewer in a database that automatically recorded the corresponding ATC (Anatomical Therapeutic Chemical) codes, revision 2009. Diagnoses relating to 100 diseases[2] were coded by a trained archivist using the 9th revision of the International Classification of Diseases.[15] Patients with the following ICD codes were classified as anxious: 300.0 anxiety states; 300.2 phobic disorders; 300.3 obsessive-compulsive disorders; 300.5 neurasthenia; 300.8 somatoform disorders; 306.2 psychogenic disease related to underlying physiological disorders. Patients with the following ICD codes were classified as depressive: 296.3

major depressive disorder, recurrent episode; 296.5 bipolar disorder, most recent episode depressed; 296.1 manic disorder; 296.6 manic-depressive psychosis; 300.4 dysthymic disorders; 300.5: neurasthenia; 309.0 adjustment reaction, 309.1 prolonged depressive reaction, 311.9 unclassified depressive disorders. Patients were considered as experiencing sleep disorders if their diagnoses related to ICD codes 307.4 (specific disorders of sleep of non-organic origin) and 780.5 (sleep disturbances).

Comorbidity was defined as the presence of at least one diagnosis other than the principal motive for consultation at the recruitment visit. Comorbidities were categorised as: co-associated sleep, anxiety, or depressive disorder (other than the main reason for consultation), musculoskeletal disorders, respiratory diseases, cardiovascular and metabolism disorders, diabetes, thyroid and endocrine disorders, and finally digestive disorders. Severity of SADD was characterised firstly by degree of quality of life (QoL) impairment, then by the presence and finally by number of associated comorbidities.

Statistical analysis

Characteristics of non-participants (age, gender, length of time attending the GP's medical practice, type of health insurance and main reasons for consultation) were used to calibrate the final sample as previously reported[2] to ensure that it would closely represent the whole population attending French GPs practices, using a method known in demographic studies as the CALMAR procedure.[16] Overall characteristics of patients seeking access to each of the three types of GP and results reported here were based on weighted data. Distributions were compared using Chi-Square and Fisher tests for categorical variables and Student and Wilcoxon tests for continuous variables.

Multiple logistic regression analyses were used to compare patients in the GP-CM group to GP-Mx and GP-Ho groups for categorical variables and were adjusted for all variables listed in Table 1 to control for potential confounding.

The GP-Mx and GP-Ho groups were compared to the GP-CM group for patients' exposure to antidepressants (ATC codes beginning with N06AB, N06AX, N06AA and N06AF), anxiolytics and hypnotics (ATC codes beginning with N05BA, N05BB, N05BX, N05BE, N05CD, N05CF and N03AE) mood normalisers (N05AN, N03AG) and antipsychotics (ATC codes beginning with N05AK, N05AA, N05AB, N05AC, N05AD, N05AF, N05AG, N05AH, N05AL, N05AX, N07XX) as well as homeopathic preparations specifically prescribed for SADD symptoms.

ANCOVA analyses were performed to provide mean scores for the SF-12 mental (MCS) and physical scales (PCS) adjusted for age (<40, 40-60, 60+ years), gender, marital status, employment status, body mass index (BMI), number of associated comorbidities (other than SADD), and finally associated SADD (other than the main diagnose, yes/no). MCS score and PCS score were categorised into quartiles corresponding to: 34.1 (Q1), 42.4 (Q2), and 48 (Q3) for MCS; 39.3 (Q1), 47.3 (Q2) and 54.2 (Q3) for PCS.

Associations between scores from each of the 17 questions of the CAMBI questionnaire and the probability of attending a GP-Mx or GP-Ho as compared to a GP-CM were computed after adjusting for age, gender and educational level. Scores obtained per question, ranging from 1 (totally disagree) to 7 (totally agree), were dichotomised in order to further distinguish participants clearly in favour (scoring 5 to 7) or in disagreement (scoring 1 to 3) with the 17 CAMBI questions. Each of the three subscales scores and the total CAMBI score were then dichotomised according to the 75th percentile (40, 26 and 33, respectively; 96 for the total score).

The possibility of a clustering effect at the practice level was tested using Generalised Estimating Equations (GEE) multivariate models. All the analyses were performed with SAS software version 9.1 (SAS Institute, Inc., Cary, North Carolina).

The study was approved by the French National Data-Protection Commission (CNIL) and the CNOM. Participating physicians received compensation fees for recruiting patients but not patients.

RESULTS

A total of 825 GPs participated in the survey. There was no difference between the three groups of GPs for age (mean = 50.7 years) but GP-Ho and GP-Mx were more often women than GP-CM (48.9% and 31.5% versus 20.3%, respectively), and less often salaried (14.3% and 16.9% versus 34.5%, respectively). In addition, GP-Ho were more likely to practise alone than GP-CM and GP-Mx (72.4% versus 51.8% and 55.9%, respectively) (all differences statistically significant). Among the 11 701 patients attending the doctor's office on the survey day, 8652 (73.9%) agreed to participate and complete information was collected for 8559 (73.1%) patients. Compared to non-participants, participants were more often women (62.7% and 56.8%, respectively), younger (mean age 43.3 and 47.7, respectively) and more likely to consult for a SADD (20.6% and 11.6%, respectively). Of the 6379 who declared the consulting physician as their regular GP, 1572 met the inclusion criteria and were included in the analyses with the following diagnoses: anxiety (n=370), depression (n=583), sleep disorders (n=480) or SADD of undetermined cause (n=139).

Compared to the GP-CM group, patients from the GP-Mx group showed similar characteristics but those from the GP-Ho group were more frequently younger, more educated, employed women living with children or a spouse (Table 1). They also had a healthier lifestyle with lower BMI, and were more frequently non-smokers and occasional or non-consumers of alcohol. They declared however less visits to their regular GP in the previous year. Motives of consultation showed more anxiety and less depression in the GP-Ho group than in the two others but the distribution was unremarkable otherwise. Physicians prescribing preferences were confirmed with the GP-Ho group using more homeopathy and less psychotropic drugs than the two other groups. The GP-Mx group however did not differ much from the GP-CM group.

Table 1. Characteristics of patients seeking care for SADD according to the type of practice of their regular GP (EPI3 Survey, n=1572)

	GP-CM (n=410) N, weighted %	GP-Mx (n=718) N, weighted %	GP-Ho (n=444) N, weighted %
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Gender						
Females vs. Males	269	64.7	500	68.9	323	72.6*
Age categories (years)						
18-39	92	20.7	195	26.7	131	28.8*
40-59	163	38.9	298	41.3	193	43.6*
60 and over	155	40.4	225	32.0	120	27.6*
Employment status						
Employed	171	39.5	353	48.9	240	53.5*
Educational level						
Secondary school not completed	93	22.1	177	22.9	158	35.2*
Universal Health Insurance coverage (CMU)						
	36	9.5	65	9.8	26	6.5
Familial status						
Living with children	164	38.1	306	42.5	195	44.1*
Living with a spouse	239	56.6	439	61.2	285	64.0*
Body Mass Index (%)						
<25	216	52.1	413	57.9	302	67.9*
25-30	124	30.9	186	25.6	106	24.0*
>30	70	17.0	119	16.6	36	8.1*
Tobacco consumption (%)						
Never smoked	195	48.4	365	50.8	251	57.1*
Past smoker	111	26.9	170	23.6	112	24.6*
Current smoker	104	24.8	183	25.6	81	18.3*
Alcohol Consumption (%)						
Never	152	37.4	287	40.0	142	32.4
Sometimes	193	46.4	354	49.3	254	56.2
Daily	65	16.3	77	10.7	48	11.4
Physical exercise (%)						
> 30 minutes / day	125	30.7	207	29.3	140	31.6
Number of visits to regular GP during the last year						
None	7	1.7	16	2.3	10	2.2
1-6	228	55.4	405	57.0	296	66.8*
7-12	142	34.6	234	32.1	114	25.6*
12 and over	33	8.4	63	8.7	24	5.4*
Number of visits to a specialist during the last year						
None	105	25.8	200	28.0	113	25.6
1	114	27.0	206	28.6	137	31.2
2	63	15.6	133	18.4	82	18.1
2+	128	31.5	179	25.0	112	25.1
Motive for consultation (ICD-9)						
Anxiety	79	18.8	158	21.2	133	30.2*
Depression	171	41.1	284	39.6	127	28.7*
Sleep disorders	131	32.7	198	28.9	151	34.0
Unspecified	52	12.6	95	12.5	65	14.1
Treatment						
Any psychotropic drugs	266	64.0	404	55.4	138	31.2*
<i>Antidepressants</i>	152	36.0	231	31.5	73	16.5*
<i>Anxiolytics/hypnotics</i>	185	44.8	286	39.3	87	19.8*
<i>Antipsychotics</i>	11	3.1	25	3.5	10	2.4
<i>Normothymics</i>	16	3.9	7	1.1	20	4.6
Other conventional drugs	144	36.0	289	41.2	189	42.7
Homeopathic medicines for SADD	1	0.2	36	4.9	139	30.9*
Other homeopathic medicines	6	1.4	58	7.8	288	67.7*

Abbreviations: GP-CM: general practitioner strictly practising conventional medicine; GP-Mx: general practitioner with mixed practice; GP-Ho: general practitioner with a certification in homeopathic care.

*Difference with conventional medicine category statistically significant ($p \leq 0.05$) in logistic regression including all variables.

Considering the severity of mental health problem, the GP-Mx group had systematically less often an associated SADD comorbidity than in the two other groups but the distribution of comorbidities other than SADD was unremarkable otherwise between groups (Table 2). For quality of life, the mental score summary (MCS) of the SF-12 was similar across the three groups with no clinically or statistically meaningful difference (Table 3). The GP-Ho group however had a slightly better physical summary score (PCS) than the two other groups.

Table 2. Burden of associated comorbidity and other psychological distress in patients with sleep, anxiety, or depressive disorders according to the type of practice of regular GPs (EPI3 Survey, n=1572)

Comorbidities present at the medical visit	GP-CM Weighted%	GP-Mx Weighted%	Gp-Ho Weighted%
Patients with SADD (n=1572)*	n=410	n=718	n=444
Associated SADD comorbidity (other than primary)	7.4	2.6 ⁺	5.3
At least one other comorbidity	74.3	68.7	69.5
MSD	27.1	23.8	24.8
Respiratory diseases	16.6	11.7	18.5
Cardiovascular and metabolism disorders	35.1	30.2	22.9 ⁺
Diabetes, thyroid and endocrine disorders	12.7	9.6	8.1
Digestive disorders	11.9	11.5	11.5
Patients with depression (n=583)	n=171	n=285	n=127
Associated SADD comorbidity (other than depression)	13.7	3.7 ⁺	10.0
At least one other comorbidity	75.2	67.3 ⁺	70.6 ⁺
MSD	29.2	23.2	28.6
Respiratory diseases	15.3	9.8 ⁺	12.8
Cardiovascular and metabolism disorders	36.5	30.4	21.6 ⁺
Diabetes, thyroid and endocrine disorders	13.0	10.8	7.9 ⁺
Digestive disorders	10.4	9.0	10.6
Patients with anxiety (n=370)	n=79	n=158	n=133
Associated SADD comorbidity (other than anxiety)	12.9	5.7 ⁺	13.6
At least one other comorbidity	71.2	72.2	62.2 ⁺
MSD	22.5	26.5	25.2
Respiratory diseases	14.3	9.8	14.2
Cardiovascular and metabolism disorders	23.6	31.2 ⁺	22.3

<i>Diabetes, thyroid and endocrine disorders</i>	10.7	11.7	9.3
<i>Digestive disorders</i>	18.1	15.0	13.7
Patients with sleep disorder (n=480)	n=131	n=198	n=151
Associated SADD comorbidity (other than sleep disorder)	9.8	3.7	9.7
At least one other comorbidity	71.3	63.6	67.6
<i>MSD</i>	29.7	22.0	21.9 ⁺
<i>Respiratory diseases</i>	14.3	12.7	21.2
<i>CV and metabolism disorders</i>	37.8	28.9	19.4
<i>Diabetes, thyroid and endocrine disorders</i>	10.4	5.6 ⁺	4.4 ⁺
<i>Digestive disorders</i>	10.2	10.7	12.1

Abbreviations: GP-CM: general practitioner strictly practising conventional medicine; GP-Mx: general practitioner with mixed practice; GP-Ho: general practitioner with a certification in homeopathic care; MSD: musculoskeletal disorders; SADD: sleep, anxiety or depressive disorders.

*Including missing diagnosis (according to ICD9) values (n=139 patients).

+Difference with conventional medicine category statistically significant ($p \leq 0.05$) in logistic regression including age (<40, 40-60, 60+ years), gender, marital status, employment status, BMI (body mass index: <25; 25-30; >30kg/m²), MCS: SF12-Mental Component Summary score; PCS: SF12-Physical Component Summary score.

Table 3. Adjusted quality of life (MCS and PCS) of patients visiting their regular GP according to the type of practice (EPI3 Survey, n=1572)

Quality of Life SF-12		GP-CM Mean (sd)*	GP-Mx Mean (sd)*	p-value*	GP-Ho Mean (sd)*	p-value*
SADD						
	MCS	35.3 (1.0)	35.9 (1.0)	0.64	36.4 (1.0)	0.24
	PCS	42.3 (1.0)	42.9 (1.0)	0.58	45.4 (1.0)	<0.001
Anxiety						
	MCS	36.7 (1.4)	35.8 (1.2)	0.73	37.3 (1.2)	0.88
	PCS	44.1 (1.4)	44.8 (1.2)	0.81	47.4 (1.3)	0.03
Depression						
	MCS	34.5 (1.4)	34.6 (1.5)	0.99	34.0 (1.6)	0.92
	PCS	40.5 (1.5)	41.9 (1.5)	0.29	44.1 (1.6)	0.006
Sleep disorders						
	MCS	34.6 (1.6)	37.0 (1.6)	0.06	35.7 (1.7)	0.64
	PCS	44.4 (1.6)	44.3 (1.7)	0.99	47.5 (1.7)	0.03

Abbreviations: GP-CM: general practitioner strictly practising conventional medicine; GP-Mx: general practitioner with mixed practice; GP-Ho: general practitioner with a certification in homeopathic care; MSD: musculoskeletal disorders; MCS: SF12-mental component summary score; PCS: SF12-physical component summary score SADD: sleep, anxiety or depressive disorders.

*from ANCOVA adjusted for age (<40, 40-60, 60+ years), gender, marital status, employment status, BMI, number of associated comorbidities (other than main SADD), SADD comorbidity (yes/no); a higher score indicates better health.

The attitudes towards complementary medicine estimated by CAMBI (Table 4) showed that patients in the GP-Ho group had a probability of scoring high (favourable to CAM) over three times that of the GP-CM group (Odds ratio (OR) = 3.65, 95% confidence interval (CI): 2.94-3.77). The result was consistent for each of the three CAMBI subscales with OR= 2.08 (95% CI: 1.78-2.32) for belief in natural treatment, OR= 1.43 (95% CI: 1.23-1.77) for active patient's participation in care, and OR= 2.75 (95% CI: 2.55-3.24) belief in holistic medicine. CAMBI scores from patients of the GP-Mx group were comparable to the GP-CM group, although a slightly higher trust in natural treatment subscale was observed (OR = 1.15, 95% CI: 1.03-1.26).

Table 4. Attitudes of patients with SADD towards complementary medicine as measured by the CAMBI (attitudes towards complementary and alternative medicine beliefs inventory) questionnaire (EPI3 Survey, n=1572)

	Type of practice	
	GP-Mx vs. GP-CM OR* (95% CI)	GP-Ho vs. GP-CM OR* (95% CI)
1. Treatments should have no negative side effects	1.11 (0.94-1.33)	1.70 (1.43-1.93)
2. It is important to me that treatments are not toxic	0.85 (0.65-1.14)	1.55 (1.41-2.03)
3. Treatments should only use natural ingredients	1.07 (0.97-1.08)	2.02 (1.87-2.47)
4. It is important that treatments boost my immune system	1.12 (0.93-1.18)	1.65 (1.38-2.11)
5. Treatments should allow my body to heal itself	1.28 (1.13-1.38)	2.02 (1.77-2.18)
6. Treatments should increase my natural ability to keep healthy	1.05 (1.01-1.34)	1.54 (1.64-2.27)
7. Treatment providers should treat patients as equals	1.01 (0.89-1.17)	1.24 (1.08-1.67)
8. Patients should take an active role in their treatment	0.88 (0.81-1.06)	1.75 (1.18-1.81)
9. Treatment providers should make all decisions about treatment	0.85 (0.74-1.07)	1.37 (1.21-1.54)
10. Treatment providers should help patients make their own decisions about treatment	0.94 (0.86-1.11)	2.43 (1.89-2.43)
11. Treatment providers control what is discussed during consultations	1.04 (0.85-1.19)	1.37 (1.18-1.45)
12. Health is about harmonising your body, mind and spirit	1.08 (0.95-1.20)	2.33 (1.55-2.45)
13. Imbalances in people's lives are a major cause of illness	1.15 (1.02-1.27)	2.07 (1.66-2.07)

14. Treatments should focus only on symptoms rather than the whole person	0.82 (0.78-1.04)	2.44 (1.75-2.45)
15. Treatments should focus on people’s overall well-being	1.21 (1.01-1.44)	1.53 (1.48-1.95)
16. I think my body has a natural ability to heal itself	1.13 (0.95-1.22)	2.43 (1.70-2.22)
17. There is no need for treatments to be associated to natural healing power	1.00 (0.77-1.07)	1.56 (1.33-1.81)
CAMBI Total score >Q3	1.05 (0.92-1.29)	3.65 (2.94-3.77)
CAMBI sub-scores:		
• Natural treatment >Q3	1.15 (1.03-1.26)	2.08 (1.78-2.32)
• Patient’s participation >Q3	0.95 (0.81-1.03)	1.43 (1.23-1.77)
• Holistic medicine >Q3	1.15 (0.95-1.17)	2.75 (2.55-3.24)

Abbreviations: GP-CM: general practitioner strictly practising conventional medicine; GP-Mx: general practitioner with mixed practice; GP-Ho: general practitioner with a certification in homeopathic care; OR: Odds ratio

*adjusted for age, gender and educational level.

DISCUSSION

To our knowledge, the EPI3 study is the first nationwide survey conducted in a large representative sample of patients to provide characteristics and attitudes, as well as the first to quantify quality of life and the burden of sleep, anxiety or depressive disorders (SADD) in patients seeking care from their regular GPs with different preferences towards CAM and homeopathic practices.

Our results suggest that patients experiencing SADD, and who chose a GP with a clear orientation towards homeopathy, differed in their socio-demographic profile but not in the severity of their mental illness from those attending regular GPs with prescribing preferences towards conventional psychotropic drugs. Patients with SADD attending a GP-Ho in our study were more likely to be female, as previously reported[17-20] except for one survey,[21] and younger. Association with age been suggested by other authors,[22] although no such association has been described elsewhere.[17,19,21]

Patients seeking care from a GP-Ho and to a lesser extent from GP-Mx, had healthier lifestyles as shown by a lower BMI and the higher number of patients that never smoked in this group, a finding that has been noted previously.[23] Greater health awareness might not only be a driver for

consulting a CAM provider but also for changing from a GP-CM because of dissatisfaction with care.[24] In these circumstances, health awareness might be a proxy variable to several other motivations including a desire for shared decision making.[25] As noted by other authors, the directionality of the relation between healthy lifestyle and consulting a GP-Ho could go in the opposite direction, with CAM utilisation [26] and interaction with a CAM practitioner [27] promoting a healthier lifestyle. More longitudinal research is needed to clarify these associations.

The higher educational attainment found among patients seeking mixed and homeopathic GPs has also been previously reported in some studies [17,19] but not in others.[20,21] More educated people may be more knowledgeable about the side effects of conventional psychotropic drugs and hence more likely to seek alternative treatments as suggested by Mac Lennan et al.[18]

With regard to the medical conditions, the EPI3 survey is one the few studies highlighting that sleep, anxiety and depressive disorders show similar burdens in terms of severity and impact on mental impairment regardless of practice modalities of GPs. As for prevalence, anxiety was confirmed as the most frequent mental health disorder encountered by alternative medicine practitioners, as previously reported.[5,10] Higher prevalence of patients suffering from depression seeking GP-CM might be attributed to the older age structure observed in this group when compared to those consulting GP-Ho: age trajectories observed for depression are often the opposite as those found for anxiety.[28] In spite of the fact that patients with depressive disorders in our study were less likely to seek strictly homeopaths than GP-CM, we must remember that depression is also one of the most commonly treated complaints as previously described for outpatient clinics of homeopathic hospitals in the UK National Health Service.[29]

Studies examining representative samples of general population seeking care for SADD have consistently shown that a large proportion of subjects are not treated with psychotropic drugs.[30,31] Conversely, psychotropic drugs use is frequently reported by subjects without identified psychiatric disorders.[32] This latter observation is probably the reason why there is an

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3 increasing trend for patients falling into the mixed category with similar characteristics and SADD. It
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5 is as if they sought a combination of both homeopathy and conventional medicines to fulfil
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7 individualised and holistic therapies needs and expectations, whilst being sure that good standards of
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9 medical and scientific practice were met.[33] This type of patients seems to be primarily concerned
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11 by associating their need for care and adequate treatment. One third of the patients with SADD
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13 consulting a GP-Mx received concomitantly homeopathic medicines and a psychotropic drug: this
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15 might suggest that homeopathic medicines could be prescribed not only as a substitute of
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17 unnecessary conventional psychotropic drugs, but also viewed as an adjunct to efficient psychotropic
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19 drugs;[10,20,34] such combination has been found to potentially help patients to accept and
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21 improve their symptoms[35] whilst avoiding some possible side effects of additional conventional
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23 therapies. Although no conclusions can be drawn at this stage on the outcome of consultations to
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25 GP-Mx and GP-Ho and whether their patients were given adequate treatment, our study highlights a
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27 genuine will from GP-Mx and GP-Ho to tailor therapies to their patients while avoiding unnecessary
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29 prescriptions.
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33 High CAMBI scores, representing greater trust and belief in CAM, were found in the GP-Ho group,
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35 particularly in the subscales related to belief in natural treatments and holistic medicine and to a
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37 lesser degree in the patient's participation subscale. Patients of the GP-Mx group exhibited only a
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39 modest preference for natural treatments and holistic medicine with no difference overall towards
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41 patients seen by physicians who practise strictly conventional medicine. The different findings might
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43 be explained by the fact that GP-Ho operate a labelled practice in France (they must be certified
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45 homeopaths) which is not the case for the GP-Mx group defined specifically for this study. Our results
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47 provide interesting evidence of criterion validity for the CAMBI scale outside the United Kingdom. As
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50 for the quality of life scale (SF-12), patients scored similarly on the mental health subscale across all
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52 three groups of GPs, a result that was consistent with the similar number of comorbidities declared
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54 by treating physicians. Some studies found that patients seeking CAM therapies showed more QoL
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56 impairment than patients seeking conventional therapies.[36] Other studies, including ours, suggest
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that, despite the modality of practice (CAM or conventional therapies), GPs treat patients exhibiting similar mental health problems and disease burden.[37]

Around 75% of patients who sought GPs exhibited additional morbidities in the EPI3 survey. The role of comorbidity in producing further burden from sleep, anxiety and depressive disorders has not been studied in patients attending GPs practising different modalities of treatment.[38,39]

Integrating research to understand the role of comorbidity in QoL is challenging due to differences across studies in QoL conceptualisation, validity of QoL measurement, recruitment context (e.g., epidemiological, treatment-seeking), and consideration of socio-demographic and clinical predictors. Studies generally account for a limited range of comorbidity attributes, typically the presence versus absence of comorbidity, which loses the richness of information inherent in psychiatric presentations.

Together with a lower number of visits to GPs and a lower proportion of prescribed psychotropic drugs in the GP-Ho group, our findings may have relevant public health implications. For instance, the National Institute for Health and Clinical Excellence (NICE), highlighted recently that the severity of depression at which antidepressants show consistent benefits over placebo is poorly defined, emphasising that, in general, the more severe the symptoms, the greater the benefit.[40] A patient-level meta-analysis demonstrated a lack of efficacy for antidepressants in the majority of patients with anxiety and depressive disorders.[3,4] Thus, the real impact of conventional antidepressants in this population is considerable, with adverse reactions outweighing potential benefits.[41] The patient's dissatisfaction with psychotropic drugs is one of the reasons cited for seeking other treatment options[42] and patients with a history of depression are more likely to seek CAM than those who have never been depressed before.[43]

Under a primary care system designed for acute rather than chronic care, where clinicians "routinely experience the tyranny of the urgent", [44] our results suggested that management of SADD by GP-Ho was associated with less visits to the GP in the previous year but no more consultations to specialists than GP-CM. Medico-economic studies are needed to assess the patterns of access to and

management by these different practitioners, which would contribute to better plan resource allocation for mental health services and target key groups for interventions in prevention, as far as severity of SADD is concerned.

Strengths and limitations of the study

The present study examined a relatively large number of primary care practices in order to provide a real-world picture of CAM and homeopathic practice within the French primary care setting. The main strengths of the EPI3 survey have already been acknowledged elsewhere.[2] These include high representativeness of the patients involved and comparability against other nationwide studies. The weighted geographical distribution of the participating GPs in the survey was similar to the national distribution of GPs in private practice across the 22 French regions surveyed, and the distribution of physicians’ individual characteristics regarding age, gender, type of contract with national health insurance and modality of practice differed only slightly from national statistics.[45]

The main limitation of our study relates to its cross-sectional design which does not allow addressing the directionality of the associations described between patients’ characteristics and their physician’s choice of medical practice. Another limitation relates to the classification of GPs, which relied on self-reporting of CAM prescriptions. The definition of GP-Ho was more accurate and based on their professional certification. Therefore, generalisations of the results must be made cautiously, since our findings represented general practice in France. Nevertheless, this particular setting can be otherwise interpreted also as a strength, because it provided a unique opportunity to compare head-to-head primary care practices differing only by preferences for homeopathy and CAM, whereas all participant physicians shared similar medical professional status and basic training in conventional medicine. We feel that albeit the context of the study was specific to one country, differences between the groups of patients provided reliable information on the differential utilisation of homeopathy and CAM.

Finally, the fact that the participants were recruited in primary care might have excluded people with severe psychiatric disorders. This potential bias was likely to underestimate the prevalence of

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3 psychotropic drug use. However, prescriptions for psychotropic drugs were similar to those found in
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5 other French studies.[46,47]
6

7 8 **CONCLUSION** 9

10 The EPI3 survey is one of the largest studies to date conducted in general practice to describe
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12 attitudes and burden of sleep, anxiety and depressive disorders in patients seeking care from GPs
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14 with different prescribing preferences towards CAM and homeopathic practices. Our results showed
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16 that patients with SADD, while differing principally in their socio-demographic profiles and
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18 conventional psychotropic prescriptions, were actually rather similar regarding the severity of SADD
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20 in terms of comorbidities and QOL. Further research is needed to explore potential benefits, both in
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22 terms of health economics and care, of consulting GPs that combine CAM and CM daily in the clinical
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24 management of SADD.
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Competing interests

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Contributors

The work presented here was carried out with the involvement of every author. LG-B, BB, FL, FR, JM, DG, BA, GD, A-MM, MR and LA conceived both the research theme and the methods, analysed the data and interpreted the results. LG-B implemented the trial in France, analysed the data, and together with FL, PE and LA drafted and revised the paper. All members of the EPI3-LA-SER group designed the study. A Fabre and PE analysed the data. All authors have contributed to, read and approved the final manuscript. LG-B is guarantor for the study. LG-B, PE and LA had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Data sharing statement

No additional data available.

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STROBE Statement—Checklist (cross-sectional studies): ‘What drives patients with sleep, anxiety or depressive disorders to seek care from general practitioners with preference for homeopathy and other complementary medicines? Results from the EPI3 population survey’ by Lamiae Grimaldi-Bensouda et al.

	Item No	Recommendation	
Title and abstract	1	(a) Indicate the study’s design with a commonly used term in the title or the abstract	✓
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	✓
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	✓
Objectives	3	State specific objectives, including any prespecified hypotheses	✓
Methods			
Study design	4	Present key elements of study design early in the paper	✓
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	✓
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants	✓
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	✓
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	✓
Bias	9	Describe any efforts to address potential sources of bias	✓
Study size	10	Explain how the study size was arrived at	✓
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	✓
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	✓
		(b) Describe any methods used to examine subgroups and interactions	✓
		(c) Explain how missing data were addressed	N/A
		(d) If applicable, describe analytical methods taking account of sampling strategy	N/A
		(e) Describe any sensitivity analyses	N/A
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	✓
		(b) Give reasons for non-participation at each stage	✓
		(c) Consider use of a flow diagram	N/A
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	✓
		(b) Indicate number of participants with missing data for each variable of interest	N/A
Outcome data	15*	Report numbers of outcome events or summary measures	✓
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted	N/A

		estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	
		(b) Report category boundaries when continuous variables were categorized	N/A
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	N/A
Discussion			
Key results	18	Summarise key results with reference to study objectives	✓
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	✓
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	✓
Generalisability	21	Discuss the generalisability (external validity) of the study results	✓
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	✓

Symbols: ✓, checked; N/A, not applicable.

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

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What drives patients with sleep, anxiety or depressive disorders to seek care from general practitioners with preference for homeopathy and other complementary medicines? Results from the EPI3 population survey.

All changes to the manuscript originally submitted have been underlined on the revised version manuscript being currently resubmitted for easier identification

Reviewer(s)' Comments to Author:	Author's replies
GENERAL COMMENTS, TITLE & ABSTRACT	
<p>REV. #1: The type of study should be specified to "cross sectional" and the word "association" used to make it clear that no causal inference can be drawn. E.g. the aim in the abstract uses "determinants" which indicate a prospective design.</p> <p>REV. #2: The main weakness is reflected in the title as the paper claims to answer the question of what "drives" patients to seek care. The term <i>determinants</i> assumes that the factors associated with CAM use are precursors rather than products of use. Perhaps if the focus was on uncovering the profiles of people with SAAD with regards to their care-seeking choices this problem could be avoided.</p>	<p>We fully agree and had no intention of performing a longitudinal analysis with this cross-sectional design. <u>Terms have been changed as suggested and the title rephrased accordingly.</u> However, we decided to keep the verb 'seek' in the title and the text as we believe that it does not imply any directionality within analyses or interpretation of results.</p>
<p>REV. #1: The aim in the abstract and text is different. I would suggest rephrasing to something similar to: "Investigating the characteristics, health status, treatment and attitudes towards CAM for patients with SADD visiting..."</p>	<p><u>The objective has been standardised and rephrased so as to better reflect the cross-sectional nature of the study.</u></p>
<p>REV. #1: The abbreviation EPI3 is not written in full any place. I personally think EPI3 should be omitted and replaced with "this study".</p>	<p>The EPI3 abbreviation (equivalent to the name of the general study) has no other specific meaning than referring to an epidemiological survey which focussed on three groups of common motives for consultation in primary care (SADD, musculoskeletal disorders and upper respiratory tract infections). We think it is important to maintain the name of the study for citation purposes (as it is often done in other large studies).</p> <p><u>No change suggested</u> – please advise otherwise.</p>
<p>REV. #1: Sometimes the term "GP-allo" is used</p>	<p><u>Terms and abbreviations have been standardised</u></p>

instead of "GP-CM"	<u>throughout the revised manuscript.</u>
METHODS	
REV. #1: Please include a sentence or two more about how the patients choose their GP, is there any previous data suggesting that patients select GPs based on the GPs prescribing preferences?	It was the objective of the study to better understand who consults who based on utilisation of CAMs and homeopathy, as there is no information in France on how patients select their GPs. Prescribing preferences were obtained from participating physicians at the time of their inclusion in the study therefore, except for GP-Ho who are certified homeopaths, patients did not necessarily know the differences between GP-CM and GP-Mx in terms of type of practice. <u>No change suggested</u> – please advise otherwise.
REV. #1: Page 10, line 47. Propensity should be probability (I thought first that it referred to propensity scores).	<u>Change made as proposed.</u>
RESULTS	
REV. #1: It is not evident throughout the article that the comparison is between GP-CM and the two other groups. As there are few differences between GP-CM and GP mixed, this could be presented in a separate section and the rest of the text could then focus on the GP-CM vs GP-Homeo comparison.	GP-CM group is the reference against which the other two groups are compared in all analyses. <u>Changes have been made in the abstract, statistical methods and results (entirely revised – see below) sections to help clarify that aspect.</u>
REV. #1: Much of the text in the result section is repetition of what is found in the tables, presented in a way that makes it difficult to find what the main findings are. I suggest to shorten the text by only presenting the main findings.	The text has been shortened with emphasis on main findings (<u>changes have not been underlined as the whole section was shortened</u>).
REV. #1: There is no presentation of the number of GP and their characteristics. This should be included in the start of the result section.	<u>Information has been added to the first paragraph of results.</u>
REV. #1: A flow chart of the patients would be helpful. I find the CONSORT guidelines for non-pharmacological trials to be relevant for showing both patient and providers.	Given this was a general survey, specific motives for non-participation were not collected. We feel that the participation rate of 73.1% was quite exceptional considering the type of health survey and that a flow chart would not contribute to further clarify potential biases (see also below). <u>No change suggested</u> - please advise otherwise.
REV. #1: Some information about non-respondents should be given in results and	<u>Information added to the first paragraph of results.</u>

mentioned in discussion.	
DISCUSSION	
<p>REV. #2: Some mention could be made of the need to disentangle whether CAM promotes healthier lifestyles or if it only appeals to people with healthier lifestyles, or both (which based on the literature and health behavior change theory) is the more likely option.</p> <p>The literature that is consistent with this finding should be presented and discussed: Is the healthy lifestyle a product or precursor of CAM use? Can the authors speculate on this point based on previous research in this area? The “drive” part of the research question cannot really be answered (See Sirois & Gick, 2002, Sirois & Purc-Stephenson, 2008, Nahin et al. 2007, Sharpe 2007 and Willams-Peiohata 2012 for more on this issue).</p>	<p>We fully agree. <u>The cross-sectional nature of this study (as in the majority of this domain) has been highlighted in the discussion (second paragraph of the discussion).</u></p> <p>We feel that the literature suggested is not directly applicable to our setting where all consultants were physicians with various degrees of preference for utilisation of homeopathy. The article cited refers mainly to types of CAM and preferences to health consultants rather than physicians.</p> <p><u>No change suggested.</u></p>
<p>REV. #2: Why is there no discussion of the results of the CAMBI analyses? Even if only one subscale showed sig. differences the lack of differences is still worth noting. How do these results relate to previous findings on the health beliefs of CAM users and how does the historical context of the current findings compare to findings regarding health beliefs from previous research? Again though no conclusions can be made regarding how such belief differences between groups might “drive” care-seeking as there is compelling evidence to suggest that such beliefs change over the course of CAM treatment.</p>	<p><u>A section has been added to the discussion to highlight CAMBI results and their potential contribution to criterion validity outside the United Kingdom where it was first tested.</u></p>
TABLES	
<p>REV. #1: The Education variable should be presented in three categories (compulsory, middle level and higher education) in table 1.</p>	<p>In France, secondary school is compulsory (<i>lycée</i>). National statistics are dichotomised below secondary school level (compulsory education) and secondary school completed (or above).</p> <p><u>No change suggested.</u></p>

REV. #1: In table 1 , line 19, page 9, there is an error ("48.pe9"). In line 40, 46 and 51 the 31 min, 12+ could be changed to >30 / >12 or over 30/12.	<u>Typo removed and changes made as suggested.</u>
REV. #1: Table 1 could include a column with p-values	As tables 1 and 2 are already quite loaded, we feel that a superscript to indicate statistical significance is sufficient. <u>No change suggested – please advise otherwise.</u>
REFERENCES	
REV. #1: The references from 12 and onwards is wrongly numbered in the text, starting with line 43 on page 6.	<u>Thank you - References have been checked and renumbered.</u>